Analysis of pediatric adverse reactions to transfusions

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BACKGROUND: Children are known to be physiologically and biochemically different from adults. However, there are no multi-institutional studies examining the differences in the frequency, type, and severity of transfusion reactions in pediatric versus adult patients. This study aims to characterize differences between pediatric and adult patients regarding adverse responses to transfusions.

STUDY DESIGN AND METHODS: This is a retrospective data analysis of nine children's hospitals and 35 adult hospitals from January 2009 through December 2015. Included were pediatric and adult patients who had a reported reaction to transfusion of any blood component. Rates are reported as per 100,000 transfusions for comparison between pediatric and adult patients.

RESULTS: Pediatric patients had an overall higher reaction rate compared to adults: 538 versus 252 per 100,000 transfusions, notably higher for red blood cell (577 vs. 278 per 100,000; $p < 0.001$) and platelet (833 vs. 358 per 100,000; $p < 0.001$) transfusions. Statistically higher rates of allergic reactions, febrile nonhemolytic reactions, and acute hemolytic reactions were observed in pediatric patients. Adults had a higher rate of delayed serologic transfusion reactions, delayed hemolytic transfusion reactions, and transfusion-associated circulatory overload.

CONCLUSION: Pediatric patients had double the rate of transfusion reactions compared to adults. The nationally reported data on reaction rates are consistent with this study's findings in adults but much lower than the observed rates for pediatric patients. Future studies are needed to address the differences in reaction rates, particularly in allergic and febrile reactions, and to further address blood transfusion practices in the pediatric patient population.

Although the specialty of pediatric medicine has existed for more than 100 years, there remains a deficit of age-specific studies.[1] Despite efforts to address the special needs of children, guidelines are largely extrapolated from adult studies.[2] A study conducted in Finland showed a significant reduction in mortality when children were treated in pediatric units rather than in adult–child mixed wards.[3] An initiative in Canada aims to create a database of pediatric reference ranges for laboratory values called the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER). Emerging evidence from CALIPER has shown that children have a different biochemical profile when compared to adults. In fact, the only biochemical marker that appears to be consistent throughout life is bicarbonate.[4] These findings highlight the need for additional research to understand the unique characteristics of pediatric patients.

ABBREVIATIONS: AHTR = acute hemolytic transfusion reaction; CPS = Center for Patient Safety; DHTR = delayed hemolytic transfusion reaction; DSTR = delayed serologic transfusion reaction; FNHTR(s) = febrile nonhemolytic transfusion reaction(s); NHSN = National Healthcare Safety Network; TACO = transfusion-associated circulatory overload; TAD = transfusion-associated dyspnea; TTI(s) = transfusion-transmitted infection(s).

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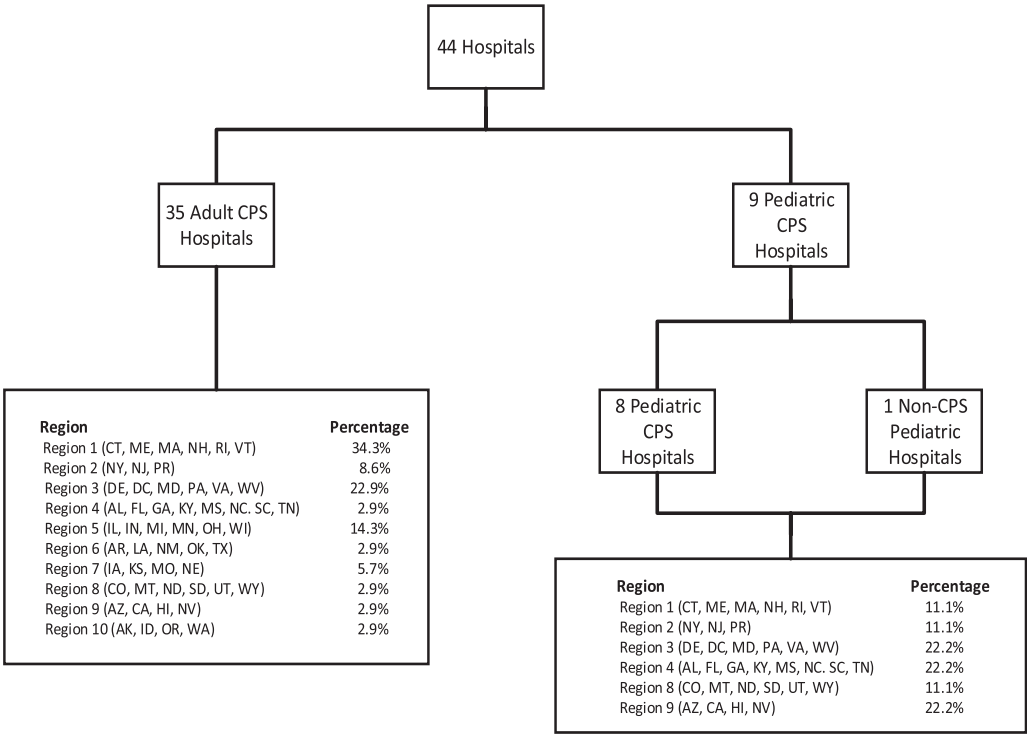

Fig. 1. Hospitals included in study.

It is, therefore, not entirely surprising to find differences between pediatric and adult patients' response to blood transfusion. A recent single-center study reported a significantly higher incidence of transfusion reactions among pediatric patients compared to adults (620 vs. 240 per 100,000 transfusions) with febrile nonhemolytic transfusion reactions (FNHTRs), hypotensive transfusion reactions, and allergic transfusion reactions as the main contributors.[5] Differences in reaction rates between pediatric and adult patients raise the question of whether transfused pediatric patients require special considerations. This study aims to expand the existing knowledge on pediatric patients' responses to blood products and to evaluate the differences within the pediatric and neonatal population with regard to transfusion reactions.

MATERIALS AND METHODS

Data collection

This retrospective data analysis of nine children's hospitals and 35 adult hospitals covered the time period from January 2009 through December 2015 for pediatric patients (under age 18) and adult patients (age 18 and over) who had a reported reaction to the transfusion of any blood component. Data were collected from adult hospitals primarily located in the following US Department of Health and Human Services Regions: Region 1 (34.3%), Region 3 (22.9%), and Region 5 (14.3%). The majority of pediatric hospitals were located in Region 3 (22.2%), Region 4 (22.2%), and Region 9 (22.2%; Fig. 1).[6] Transfusion reaction data were obtained from the Columbia University Department of Pathology and Cell Biology CoPath laboratory information system (CoPathPlus, v2013.01.1.174, Cerner Corp.) in accordance with the ethical standards of the committee on human experimentation, and approval was obtained from the institutional review board. Information collected included the number of transfusions and transfusion reactions by year, patient age, final diagnosis (reaction type), component type, and symptoms for patients treated at Children's Hospital of New York. Transfusion reaction data were also obtained from the AABB Center for Patient Safety (CPS). This database contains deidentified adult and pediatric transfusion reaction data reported by CPS member hospitals through the group function of the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) Hemovigilance Module, a voluntary national reporting system. The data reported from the member hospitals include the number of transfusions and transfusion reactions by year, final diagnosis (reaction type), component type, patient's age, and symptoms. The reactions were categorized according to the CDC's NHSN Biovigilance Component Hemovigilance Module Surveillance Protocol case definitions, severity grade, and imputability criteria for both the CPS and the non-CPS hospitals.[7] For CPS hospitals, the reaction categorization was recorded directly into the NHSN system by the hospital's blood bank staff or transfusion safety officers, usually in consultation with

a blood bank physician. Similarly, for the non-CPS hospital, reactions were classified using the same NHSN categories and definitions, but stored in a separate hospital database that did not feed into the NHSN system. The classifications were based on the transfusion reaction consultation note, which is finalized by a transfusion medicine physician. A case definition category of "definitive" implies that the adverse event meets all criteria for the diagnosis of a given reaction type; "probable" implies that the event meets specifically defined NHSN criteria but not all criteria; and "possible" implies that the reaction does not meet all criteria but that another, more specific reaction definition, does not apply.[7] An imputability category of "definite" implies that no other explanation for symptoms except the transfusion is present, "probable" implies that an alternate explanation is present but transfusion is the most likely cause of the symptoms, and "possible" implies that alternate explanations are likely but transfusion cannot be ruled out as the cause.

Denominator data included whole blood (WB)-derived and apheresis-collected components for the following types: WB, red blood cells (RBCs), platelets (PLTs), cryoprecipitate, plasma (FFP) whether thawed or fresh frozen, and granulocyte products transfused during the study time period. The aggregate denominator was calculated from hospitals reporting either pediatric or adult specific data. Adult hospitals that reported only adult adverse reactions and provided specific adult denominator data were included. Pediatric hospitals were classified as such provided their institution type was reported as a children's facility. Of these, eight hospitals with pediatric-specific denominator data and 35 hospitals with adult-specific denominator data were included in the study from the CPS database. With the addition of the non-CPS pediatric hospital and its denominator data, this resulted in data from 44 hospitals (Fig. 1).

Analysis of merged database

The AABB CPS hemovigilance database and the Columbia University database were merged to create a single data set. The aggregate pediatric data were divided into two groups: neonatal patients (under 30 days of age) and nonneonatal patients (30 days to 18 years of age). Due to the low number of reported neonatal transfusion reactions ($n = 25$), the neonatal cohort was included in the pediatric group for statistical analysis and will only be discussed descriptively. Inclusion criteria were as follows: reactions in patients under the age of 18 years (for the pediatric data); reactions in patients age 18 years and older (for the adult data); NHSN imputability categories of definite, probable, or possible; all severity grade categories; and NHSN case definition categories of definitive, probable, and possible for all reaction types except other and unknown. Reactions categorized as other and unknown can only be accorded a case definition category of "not applicable"; therefore, the case definition category of not applicable for these two reaction categories was included in the analysis. Reaction types were acute hemolytic transfusion reaction (AHTR), allergic reactions, delayed hemolytic transfusion reaction (DHTR), delayed serologic transfusion reaction (DSTR), FNHTR, hypotensive transfusion reaction, transfusion-associated circulatory overload (TACO), transfusion-associated dyspnea (TAD), transfusion-related acute lung injury (TRALI), transfusion-transmitted infection (TTI), other, and unknown. Exclusion criteria were reactions in patients age 18 years and older (for the pediatric group); data from hospitals not reporting denominators; data from hospitals not reporting components transfused by type; data from months where no denominator was reported; case definition criteria of not applicable (for all reaction types except other and unknown) or imputability categories of "doubtful," "ruled out," and "not determined." Cases excluded from pediatric hospitals because of age were not added to the adult cohort due to a lack of adult transfusion denominator data from these hospitals.

Statistical analysis was performed using computer software (SAS, Version 9.4, SAS Institute, Inc.; and R, Rv3.3.1, R Foundation for Statistical Computing). Rates are reported as per 100,000 transfusions, where a transfusion was one unit or dose of component. Calculated pediatric rates were compared to calculated adult reaction rates from the merged database. Chi-square testing was performed to test associations between patients' age group, component type, and reaction type. For reactions with expected frequencies of 5 or less, a Fisher exact test was used. All analyses employed two-tailed testing with a threshold of p value of less than 0.05 considered significant.

RESULTS

There were a total of 3822 reported transfusion reactions (3670 from the CPS data set and 152 from the non-CPS data set) from 1,222,869 transfused components during the study period. This consisted of 1402 pediatric patient reactions to 260,664 components transfused and 2420 adult patient reactions to 962,205 components transfused (Table 1). Among adult reactions, 44.4% were of definite, 32.0% were of probable, and 23.6% were of possible imputability to the transfusion. Among pediatric reactions, 37.7% were of definite, 49.2% were of probable, and 13.1% were of possible imputability to the transfusion. Significant differences between the pediatric and adult cohorts were present for definite, probable, and possible imputability categories in that adults had a higher percentage of reactions classified as definite or possible imputability while pediatric patients had more reactions classified as probable imputability ($p < 0.001$). Of the two most common reaction types, adult patients had more

TABLE 1. Aggregated number of adverse reactions, 2009 to 2015

Reaction type	Number of reactions: Pediatric patients (age < 18), 9 hospitals reporting (rate per 100,000)	Number of reactions: Adult patients (age ≥ 18), 35 hospitals reporting (rate per 100,000)
Immunologic		
Allergic	843 (323)	689 (72)
FNHTR	445 (171)	1,063 (110)
AHTR	13 (5)	8 (1)
DSTR	13 (5)	248 (26)
TRALI	4 (2)	7 (1)
DHTR	1 (<0.5)	36 (4)
Nonimmunologic		
TAD	14 (5)	63 (7)
Hypotensive	13 (5)	39 (4)
TACO	9 (3)	127 (13)
TTI	5 (2)	
Other	35 (13)	66 (7)
Unknown	7 (3)	74 (8)
Total number of reactions	1,402 (538)	2,420 (252)
Total number of units or doses transfused	260,664	962,205

FNHTR and allergic reactions classified as definite and possible; pediatric patients had more FNHTR and allergic reactions classified as probable (Fig. 2).

The observed pediatric transfusion reaction rate of 538 per 100,000 transfusions was significantly higher than the adult reaction rate of 252 per 100,000 transfusions ($p < 0.001$ Table 2). Transfusions of RBCs and PLTs were the most common components associated with any type of transfusion reaction in both the pediatric and the adult groups. More than half, 54.6%, of pediatric transfusion reactions were associated with RBC transfusions, as were 64.1% of adult transfusion reactions. PLT transfusions were associated with 40.2% of pediatric transfusion reactions and 21.8% of adult transfusion reactions. The rate of reaction per 100,000 RBC and per 100,000 PLT transfusions in the pediatric group (577 and 833, respectively) was more than double that of the adult reaction rate (278 and 358, respectively), and this difference was significant for both component types ($p < 0.001$; Table 2).

A significantly higher pediatric reaction rate was observed for AHTR, allergic, FNHTR, and other from RBC transfusion. The higher reaction rate was most pronounced with AHTRs, which had a pediatric rate of approximately 10 times that of the adult group (9.03 vs. 0.90 per 100,000, $p < 0.001$). Allergic reactions from PLT transfusions were also more common in the pediatric population (624 vs. 183 per 100,000, $p < 0.001$). There were three reaction types where adults had a significantly higher rate associated with the transfusion of RBCs: DSTR, DHTR, and TACO (Table 3).

The most commonly reported severity category for pediatric and adult patients was nonsevere (95.3 and 88.7%, respectively). There were 53 (3.78%) severe and nine (0.64%) life-threatening reactions in children compared to 135 (5.58%) and 45 (1.86%) in adults, respectively ($p = 0.016$ and $p = 0.004$). For pediatric patients, the single reported DHTR, two of the four reported TRALIs, one of the five TTIs, two of the 13 hypotensive, and three of the 843 allergic reactions were categorized as life-threatening. For adult patients, three of the seven reported TRALIs, nine of the 689 allergic reactions, eight of the 39 AHTRs, two of the 66 other reactions, 19 of the 127 TACO cases, and four of the 63 TAD cases were categorized as life-threatening (Fig. 3). There were no pediatric transfusion-related deaths reported. For adult patients, there were three reported deaths related to transfusion: one allergic reaction with probable imputability, one other reaction with possible imputability, and one TACO with possible imputability (Fig. 3).

The neonatal subset ($n = 25$) had mostly nonsevere reactions ($n = 24$; 96%), with one reaction (allergic) that was severe. Of the 24 nonsevere neonatal reactions, one was an AHTR, three were hypotensive, six were FNHTRs, three were other, one was an unknown, and 10 were allergic. There were no reported TRALI, TAD, TACO, TTI, or DSTR cases in the neonatal group.

DISCUSSION

Although it is well established that pediatric patients have unique physiologic characteristics that may affect reactions to blood products,[8,9] there are few studies characterizing specific differences. In the United States, the reported transfusion reaction rate is 250 per 100,000 for all component types, and pediatric transfusions comprise 5% of all RBC, 9.4% of all PLT, and 4.9% of all FFP transfusions.[10] The CDC reported that overall reaction rates were 219.2 per 100,000 for RBC transfusions and 430.4 per 100,000 for PLT transfusions.[11] These were not age specific

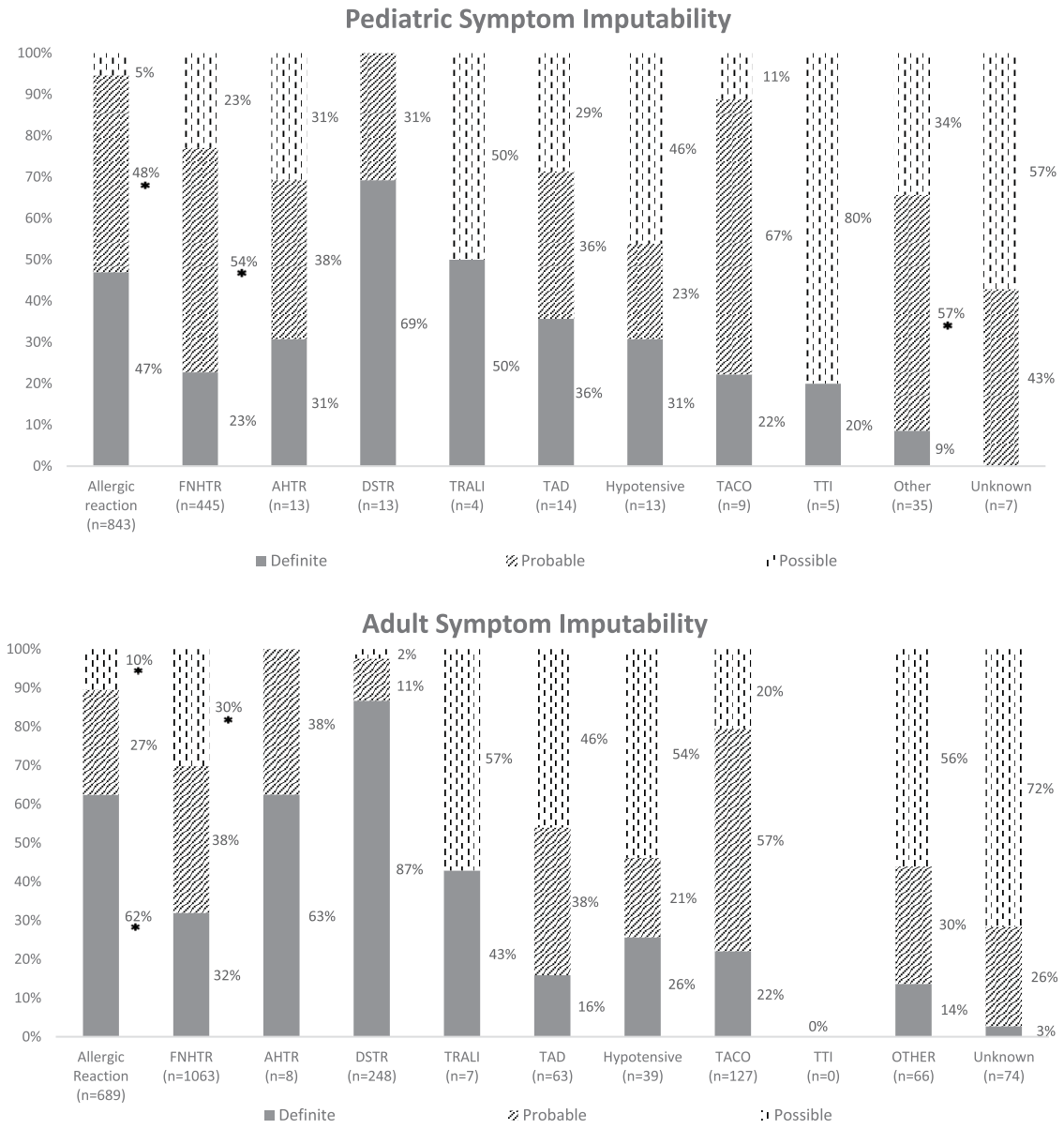

Fig. 2. Pediatric and adult adverse reaction by imputability of symptoms. DHTR reaction type had n = 1 for pediatric patients and n = 36 for adult patients and is not pictured. Percentages with an asterisk (*) denote that this category is significantly higher than the corresponding adult or pediatric category ($p < 0.05$).

TABLE 2. Comparison of adverse reaction rates by age group and component type, 2009 to 2015

Component type	Pediatric denominator*	Pediatric rate (per 100,000)	95% CI	Adult denominator*	Adult rate (per 100,000)	95% CI	p value
RBCs	132,846	577	537-619	558,206	278	264-292	<0.001
PLTs	67,737	833	766-905	147,192	358	328-390	<0.001
FFP	29,600	139	101-190	164,576	153	135-174	0.607
CRYO	30,074	3.33	0.174-21.6	90,438	6.63	2.70-15.2	0.999
Other†	407			1,793			
Total	260,664	538	510-567	962,205	252	242-262	<0.001

* n = number of units or doses transfused.
† Other includes WB, multiple component transfusions, granulocytes, unknown, and other/unspecified component types.
CRYO = cryoprecipitate.

TABLE 3. Adverse reactions by blood component type, 2009 to 2015

Component type*	Pediatric reactions†	Rate‡ per 100,000	95% CI	Adult reactions	Rate§ per 100,000	95% CI	p value
AHTR							
PLTs	1	1.48	0.08-9.59	3	2.04	0.53-6.49	0.999
RBCs	12	9.03	4.89-16.27	5	0.9	0.33-2.22	<0.001‖
Allergic reaction							
FFP	30	101	69.6-147	184	112	96.5-129	0.686
PLTs	423	624	567-687	270	183	163-207	<0.001‖
RBCs	369	278	251-308	207	37	32.3-42.6	<0.001‖
CRYO				1	1.11	0.06-7.18	
DHTR							
RBCs	1	0.75	0.04-4.89	36	6.45	4.90-9.03	0.02‖
DSTR							
PLTs				3	2.04	0.53-6.49	-
RBCs	13	9.79	5.44-17.2	242	43.4	38.1-49.3	<0.001‖
FNHTR							
FFP	6	20.3	8.24-46.5	32	19.4	13.5-27.8	0.999
PLTs	105	155	127-188	185	126	109-146	0.097
RBCs	327	246	221-275	807	145	135-155	<0.001‖
CRYO	1	3.33	0.17-21.6	3	3.32	0.86-10.6	0.999
Hypotensive reaction							
FFP	2	6.76	1.17-27.3	6	3.65	1.48-8.37	0.351
PLTs	4	5.91	1.89-16.2	10	6.77	3.45-13.0	0.999
RBCs	7	5.27	2.31-11.4	19	3.38	2.11-5.43	0.32
CRYO				2	2.21	0.38-8.92	
TTI							
PLTs	1	1.48	0.08-9.59				
RBCs	4	3.01	0.96-8.28				
TACO							
FFP				12	7.29	3.92-13.0	
PLTs	2	2.95	0.51-11.9	15	10.2	5.90-17.2	0.138
RBCs	6	4.52	1.84-10.4	88	15.8	12.6-19.4	0.005‖
TAD							
FFP	1	3.38	0.18-21.9	7	4.23	1.85-9.13	0.999
PLTs	9	13.3	6.48-26.2	17	11.5	6.92-18.8	0.89
RBCs	3	2.26	0.58-7.20	36	6.41	4.56-8.98	0.107
TRALI							
PLTs	2	2.95	0.51-11.9	2	1.35	0.23-5.46	0.595
RBCs	1	0.75	0.04-4.89	5	0.891	0.33-2.21	0.999
Other							
FFP	1	3.38	0.18-21.9	9	5.47	2.67-10.8	0.999
PLTs	12	17.7	9.60-31.9	14	9.51	5.41-16.4	0.163
RBCs	22	16.6	10.6-25.5	43	7.7	5.64, 10.5	0.004‖

* Component types of multiple, unknown, granulocytes, and other are not shown as denominator data were not available or incomplete.
† Reaction type unknown is not included.
‡ Pediatric denominators used for number of units/doses transfused: FFP, 29,600; PLTs, 67,737; RBCs, 132,846; CRYO, 30,074.
§ Adult denominators used for number of units/doses transfused: FFP, 164,576; PLTs, 147,192; RBCs, 558,206; CRYO, 90,438.
‖ Significant p values.
CRYO = cryoprecipitate.

and, as this multicenter study highlights, may not be applicable to the pediatric population. Our findings are consistent with a previous single institution study that analyzed pediatric reactions and reported a rate of 620 per 100,000.[5] The pediatric population appears to have a reaction rate more than two times that of adults.

Established databases in other countries have been tracking pediatric transfusion reaction data on a large scale. In the UK Serious Hazards of Transfusion (SHOT) system, reactions resulting in serious harm or death and near miss events that could have resulted in such an event are analyzed. For these events, an estimated overall

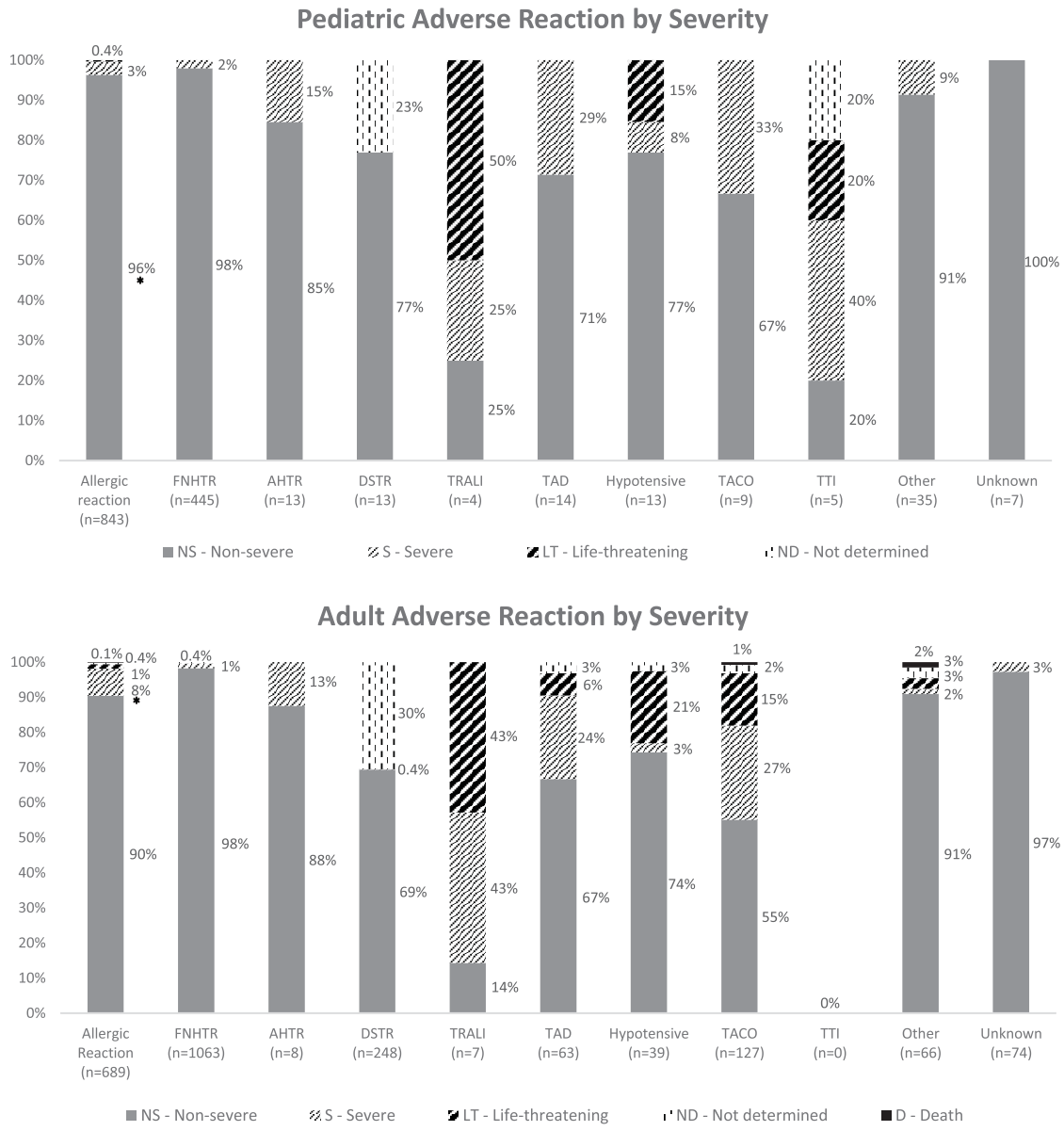

Fig. 3. Pediatric and adult adverse reaction by severity. DHTR reaction type had n = 1 for pediatric patients and n = 36 for adult patients and is not pictured. Percentages with an asterisk (*) denote that this category is significantly higher than the corresponding adult or pediatric category ($p < 0.05$).

pediatric risk of 62.5 per 100,000 components issued in the United Kingdom was reported.[12] This figure is higher than the risk of severe or life-threatening events observed here, 23.8 per 100,000, likely attributable to the lack of near miss events in this database. In the Norwegian System (Troll), the reporting of serious adverse events and serious reactions is mandatory and annual reports have been published since 2004.[13] The Troll system has not tracked nonsevere reactions since 2010; before that, when the system tracked all reactions, an all-ages all-reaction rate was cited at 147 per 100,000 components transfused.[13] The hemovigilance system in Denmark, the Danish Registry of Transfusion Risks (DART) and the Transfusion and Transplantation Reactions in Patients (TRIP) reporting system of the Netherlands similarly do not report pediatric specific data.[14,15] Due to the differences in reporting and data collection of these systems, it is difficult to make direct comparisons or draw conclusions.

Within the pediatric population, allergic reactions to PLTs and RBCs were the most frequently reported reaction types. The rate of allergic reactions to PLTs was more than three times the adult rate, and the rate of allergic reactions to RBCs was more than seven times the adult rate. National reaction rate data cite the allergic reaction rate

as 53.6 per 100,000 RBC transfusions and 302 per 100,000 PLT transfusions.[16] These estimates are higher than the adult rates observed in this study but lower than pediatric allergic reaction rates of 278 per 100,000 RBC transfusions and 624 per 100,000 PLT transfusions reported here. Febrile reactions to RBC transfusions, the second most common reaction type, follow a similar pattern. The nationally reported rate for FNHTRs, 106.3 per 100,000 RBC transfusions, reflects our observed adult rate of 145 per 100,000 RBC transfusions, but is lower than our observed pediatric rate of 246 per 100,000 RBCs transfused. Why pediatric patients have a significantly higher rate of allergic and febrile reactions is not clear. Pediatric patients may have different physiology that predisposes them to these reactions. It is also possible that pretransfusion medication practices differ between the pediatric and adult populations. However, past studies have shown routine pretransfusion medication does not make a difference in reaction rates for children.[17] Finally, it cannot be excluded that differences in the intensity of monitoring by pediatric health care providers or the patient's family members at bedside might contribute to increased reporting of suspected reactions. The symptom imputability of definite was seen significantly less frequently for the pediatric population in FNHTR and allergic reactions. This category means no other explanation for symptoms was present. This suggests that adult patients may have more readily observable and distinct symptoms, that adult patients are more able to describe their symptoms, or that reporting practices may differ between the pediatric and adult population.

The higher pediatric rate of AHTR in response to RBC transfusions, while few in number (12 pediatric vs. 5 adult), was significant. Caution should be used when drawing conclusions from this comparison because there are a small number of cases and the imputability of possible was present in four of 12 pediatric cases involving RBCs and none of five adult cases. This category means that alternate causes of hemolysis are more likely but transfusion cannot be ruled out. Of the pediatric reactions, only six had identifiable antibodies: an anti-A in an ABO group A newborn, a warm autoantibody in a 1-year-old patient, and four patients with a nonspecific antibody. The remaining six patients did not have identified antibodies and the reactions were classified as non–immune-mediated hemolysis. In the adult population, two of the five AHTRs had identifiable antibodies on workup: an anti-VW and an autoantibody identified as an anti-Ku. The remaining three adult patients had nonspecific antibodies. None of the adult cases were classified as non–immune mediated. Perhaps there is an underreporting of non–immune-mediated hemolysis in adults given the fact that there were no reported cases.

It is notable that TACO and both types of delayed reactions (DSTR and DHTR) had a higher incidence in the adult group. It is not surprising that adults have a higher rate of TACO considering the prevalence of heart disease and the concomitant decreased ability to cope with volume shifts. However, the differences in the delayed reaction types are more unexpected. To our knowledge, the reported probability of antibody formation after exposure to donor RBC antigens (2%-6% in patients receiving RBC transfusions) is the same for pediatric patients (over the age of 4 months) as for adults.[8] If pediatric patients have a similar rate of alloimmunization, then the higher reaction rate observed in the adult population of delayed transfusion reactions is unanticipated. One possibility is that the delayed reactions are secondary to anamnestic responses and that chronically transfused adults, having had greater opportunity for alloimmunization, have a greater risk for delayed reactions. Another contributing factor may be hospital differences in prophylactic RBC antigen matching. The practice of prophylactic antigen matching for chronically transfused patients became commonplace after a landmark study in 2001, which showed that Rh and Kell antigen matching of blood products in pediatric patients with sickle cell disease decreased alloimmunization from 3% to 0.5% per unit.[18] Despite this publication, as late as 2005, only 37% of laboratories reported phenotyping nonalloimmunized patients with sickle cell disease,[19] and routine RBC antigen matching has remained variable between transfusion services as recently as 2011.[20] Therefore, it may be that pediatric blood banks are more likely to provide antigen-matched RBCs, thus the lower rate of DSTR and DHTR in this population. Indeed, the non-CPS pediatric hospital included in this study has a policy to prophylactically antigen match for sickle cell patients; however, the extent of this practice is unknown for the CPS hospitals. It is important to bear in mind that the data may reflect a reporting bias. Pediatric DSTRs and DHTRs were frequently not captured in the reporting system for the non-CPS hospital because this system relies on provider initiation of a reaction, which rarely occurs for symptom-free events (such as DSTR), or for symptoms discovered weeks after the transfusion, such as DHTR, as the provider may not link the two events as related. The underreporting may also have occurred in the CPS hospitals that also rely on provider initiation.

The other reaction category was used significantly more in the pediatric cohort than in the adult cohort for classifying reactions to RBC transfusions. This is interesting because the other reaction category pertains to suspected reactions that do not fit into any alternative category.[7] Hyperkalemia and transfusion-associated acute gut injury may be more predominant in pediatric populations and both of these fall into the other category, according to the CDC.[7] This finding may be attributed to the difficulty young children might have in expressing their symptoms to health care providers, forcing the provider to classify the reaction based on physically observable

symptoms only. It could also reflect an overabundance of caution when transfusing RBC products to children on the part of clinical staff, where any deviation from normal may trigger a reaction report that does not meet any case definition criteria.

The nine reported life-threatening pediatric reactions did not involve any neonatal patients. The three pediatric life-threatening allergic reactions involved respiratory distress that responded to epinephrine administration. In fact, more than three-fifths (six of nine, 67%) of the pediatric life-threatening reactions involved respiratory symptoms. The single severe neonatal allergic reaction had an imputability of probable and also presented with respiratory symptoms. Of the 45 life-threatening reactions in adult patients, 35 (78%) presented with respiratory symptoms and 28 (62%) presented with cardiovascular symptoms.

This study had several limitations inherent to many pediatric observational studies. The hemovigilance database is dependent on voluntary reporting of most reaction types by the institutions, and there may be unassessed differences in the nonreporting hospitals. In addition, reactions could be underestimated or not recognized if there are no measurable hemodynamic or visibly apparent symptoms in pediatric patients who are less able to verbalize the nature of their discomfort associated with a transfusion. Although many mild allergic reactions were reported to the system, the reporting of these types of reactions is not required. Furthermore, the CDC NHSN reporting system was a limitation. When this module was created, certain reactions (TRALI, TACO, TAD, and DSTR) did not have possible or probable case definitions, meaning that these case definition descriptors were not defined for these reactions. However, the electronic reporting system did not prevent users from selecting these undefined descriptors for the case definition of these reactions. The current database no longer allows reporting of nonstandardized case definitions as of 2011. These types of reactions now classify as other or unknown.

In conclusion, this study demonstrates that pediatric patients are more likely than adults to react to blood products, with RBC and PLT transfusions associated with the greatest magnitude of observed differences. Additionally, data on neonatal transfusion reactions remain scarce despite this multiyear aggregate analysis. Understanding the differences in pediatric reactions compared to adult reactions is essential for prevention. Moving forward, additional studies are needed to understand transfusion reactions in this unique and vulnerable population.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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