RESEARCH ARTICLE

Fractures Among Inpatients in a Pediatric Hospital

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ABSTRACT

OBJECTIVE: Fractures occurring in hospitalized children may be an underrecognized preventable harm with implications for current and future bone health, but few data exist regarding the clinical characteristics of these pediatric patients. We describe the clinical characteristics of patients who sustained fractures during hospitalization over a 4.5-year period at a single tertiary care center.

METHODS: We retrospectively identified subjects who experienced inpatient fractures using a voluntary safety event reporting system and computer-assisted keyword search of the electronic medical record. We used the medical record to collect clinical characteristics, laboratory data, and survival status.

RESULTS: The safety event reporting system and keyword search identified 57% and 43% of subjects, respectively. Fifty-six subjects sustained 128 fractures while hospitalized, most frequently at the femur (33 fractures) and humerus (30 fractures). Twenty-seven subjects sustained multiple fractures. Common clinical characteristics included age ≤1 year (64%); preterm birth (53%); admission to an ICU (90%); immobilization (88%); and weight-for-age *z* score less than or equal to −2.0 (52%). Sixteen (29%) subjects died, and the mortality rate varied by primary diagnosis.

CONCLUSIONS: Critically ill, immobilized infants under 1 year of age and who were often born preterm sustained the majority of fractures occurring during hospitalization. A voluntary reporting system was insufficient to identify all inpatient fractures. Future studies should explore optimal fracture screening strategies and the relationship among fractures, severity of illness and mortality in hospitalized children.

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Fractures occurring in hospitalized children are adverse events that have implications for current and future bone health and may be preventable. Many hospitalized children exhibit risk factors for fractures, such as poor nutritional status, immobilization, and medications altering bone metabolism.[1,2]

Despite the potential impact of hospital-associated fractures on patient morbidity during hospitalization and postdischarge, fractures may be underrecognized as a hospital-associated harm. Identifying adverse events such as fractures during hospitalizations is challenging. Voluntary reporting systems are estimated to detect 10% to 20% of adverse events.[3,4] The use of pediatric trigger tools has led to increased identification of harmful events in pediatric hospitals[5] and in NICUs,[6] because trigger tools consistently identify higher rates of harm than do voluntary reporting systems. "Triggers" are specific words or phrases in the medical record resulting in a more detailed medical record review to identify whether an adverse event occurred during hospitalization. For example, the word "naloxone" could trigger a review to distinguish a clinical overdose from appropriate therapy in nonprescribed opiate use.[5] In these reports, fracture has not been included as an adverse event, and little is known regarding the prevalence of fracture or associated risk factors in hospitalized pediatric patients. Among chronically ill children, most studies of fracture risk factors and prevalence rates have been conducted in small disease-specific retrospective cohorts or in outpatients.

Delineation of the characteristics of hospitalized children who sustain fractures could inform both screening strategies to identify those patients at the highest risk for fracture and the development of trigger tools to measure fracture occurrence. Our primary aim was to describe the clinical characteristics of patients who sustained fractures during hospitalization at a single tertiary-care center over a 4.5-year period. A secondary aim was to determine how many fractures were detected using a voluntary reporting system as compared with a computer-assisted keyword search of medical records.

METHODS

Study Design and Population

We used 2 complementary methods to retrospectively identify fractures detected in patients hospitalized between January 1, 2008, and June 30, 2012, at Boston Children's Hospital (BCH), a tertiary care center. First, we identified subjects using the Safety Event Reporting System (SERS), a voluntary Web-based database used by health care providers to record adverse events within 24 hours of occurrence.[7] Beginning in 2008, a hospital-wide educational initiative encouraged reporting of inpatient fractures using SERS. In 2009, a multidisciplinary Bone Task Force at BCH was convened to identify inpatients at high fracture risk and implement a screening process to identify fractures that were noted during hospitalization. SERS recorded 40 fracture incidents among 32 unique patients for the study period.

Second, we identified subjects using Informatics for Integrating Biology and the Bedside (i2b2)[8] to conduct a computer-assisted keyword search of radiology reports and inpatient physician notes for the terms ("osteopenia" OR "osteopenic") AND "fracture" AND "portable." At the time this study was conducted, there were no search terms that could reliably distinguish inpatients from outpatients, and initial searches yielded thousands of radiographs mainly performed in outpatients. Thus, the search term "portable" was included to limit radiographs to those performed on inpatients. Forty-one of 157 patient charts found by keyword search correctly identified fractures that occurred during hospitalization and 116 charts did not include inpatient fractures. Of the 41 subjects, 24 were newly identified by i2b2, and 17 were previously found through SERS.

For the 56 subjects, we reviewed charts for characteristics including anatomic location of fractures; age; gestational age at birth; primary diagnosis; hospital location; duration of hospitalization; immobilization history; and the reason the index fracture was suspected. We recorded weight and length/height closest to and within 60 days of index fracture date, and calculated weight-for-age and length/height-for-age *z* scores using Olsen (if corrected age ≤40 weeks),[9] World Health Organization or Centers for Disease Control and Prevention growth charts.[10] We collected hospital medication exposure, including paralytics, diuretics, and parenteral nutrition. For anticoagulants, anticonvulsants and glucocorticoids, we also recorded use before hospitalization from medical records. We recorded serum levels of: total calcium and phosphorus measured by spectrophotochemical assay using Roche Cobas c501 system (Roche Diagnostics, Indianapolis, IN); thyroid-stimulating hormone (TSH), total and free thyroxine, measured by electrochemiluminescent immunoassay using Roche Cobas e701 system (Roche Diagnostics); 25-hydroxyvitamin D (25OHD), measured by liquid chromatography-tandem mass spectrometry. We recorded the 25OHD level closest to index fracture date and obtained within 90 days before or 30 days after index fracture; we excluded 1 subject with a 25OHD value >100 ng/mL due to vitamin D–dependent rickets, type II. For TSH, we recorded values obtained within 3 months of the index fracture. We recorded anatomic site and number of additional fractures detected during the same hospitalization as the index fracture(s) and recorded survival status as of June 2014. The BCH Institutional Review Board approved the study.

Statistical Analyses

Data analyses were performed by using SAS version 9.3 (SAS Institute, Cary, NC). For bivariate analyses, we used *t* tests to compare means and χ^2 test to compare proportions. Statistical significance was defined as a $P < .05$.

RESULTS

Fracture Site and Number

Fifty-six subjects sustained 128 fractures. All fractures were closed and noncomminuted. The femur was the most frequent fracture site (33 fractures in 21 subjects), followed by the humerus (30 fractures in 25 subjects; Fig 1). Twenty-nine subjects sustained a single fracture. Twenty-seven subjects sustained multiple fractures, ranging from 2 to 10 fractures each (median 2 fractures, mean 3.7, SD 2.7). The mean length of hospital stay until discharge or death was

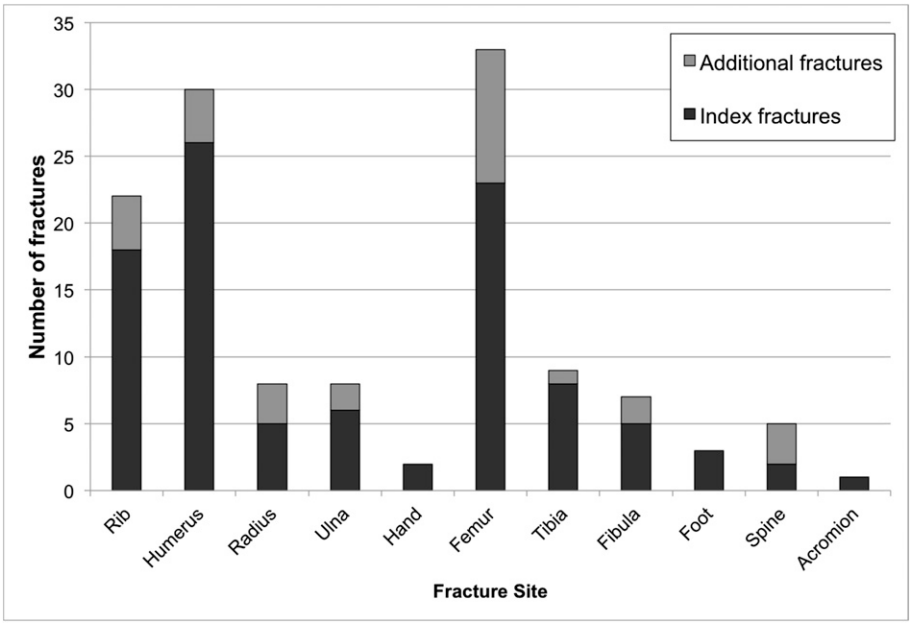

FIGURE 1 Number of fractures at each anatomic site (total 128 fractures). Distribution of fracture frequency by fracture site. Dark gray shading represents the index fracture(s), and light gray shading represents fracture(s) identified subsequent to the index fracture(s).

170 days (SD 178 days). At discovery of the index fracture (mean 71 days after admission, SD 77 days), 56 subjects sustained 99 fractures, with ≥2 index fractures in 19 subjects. Eleven subjects sustained 29 fractures after the index fracture(s), during the same hospitalization. Of the 99 index fractures, 28 fractures in 22 subjects (39%) were detected because of radiographs performed for pain complaint (16 subjects, 21 fractures), limited mobility (4 subjects, 5 fractures), or witnessed trauma (2 subjects, 2 fractures). Among 34 subjects with 71 fractures identified as incidental findings, 23 subjects had previous normal radiographs of ≥1 fracture sites performed during the same admission between 1 and 45 days earlier than the fracture detection date. One additional subject was admitted on the first day of life, and 1 subject born at 25 1/7 weeks' gestational age was transferred to BCH from another hospital at 13 days old. Thus, 25 of the 34 subjects (74%) with incidentally detected index fractures sustained ≥1 index fractures as inpatients.

Demographic and Clinical Characteristics

At the time of index fracture, 53 subjects had a chronologic age between 29 days and 15.0 years (Fig 2). Thirty-seven (64%) subjects were infants with a corrected age ≤12 months (mean 3.5 months, corrected age, SD 3.6). Admission diagnoses included congenital heart disease (CHD; $n = 13$), prematurity ($n = 12$), esophageal atresia ($n = 14$), and solid organ or bone marrow transplant (2 liver, 1 heart, 1 lung, and 1 bone marrow). Other admission diagnoses included 1 each of the following: infantile osteopetrosis, vitamin D–resistant rickets, polymicrogyria, neurodegenerative disease, malrotation, progressive familial intrahepatic cholestasis, choanal atresia, psychiatric disorder, immunodeficiency, chromosomal deletion, and epidermolysis bullosa. Three subjects with esophageal atresia, 3 with CHD, 1 with solid organ transplant, and 2 with other primary diagnoses were born preterm. Of the 3 subjects who were 25.0 to 33.4 years old, 1 had congenital heart disease and sustained a rib fracture; 1 had congenital heart disease, glycogen storage disease, and muscular dystrophy and had a rib fracture; and the third subject had spinal muscular atrophy type II and had a humeral fracture.

Most subjects (89%) were admitted to an ICU and acutely immobilized (88%) for mechanical ventilation and/or paralysis (Table 1). Seventy-five percent were ventilated for ≥2 weeks. Medication exposures included diuretics ($n = 46$, 82%), heparin or enoxaparin ($n = 14$, 25%), and, rarely, anticonvulsant ($n = 3$) or chemotherapy ($n = 1$). In the 5 years before index fracture, 28 subjects (50%) had used oral or intravenous glucocorticoids. Average duration of oral or IV glucocorticoids was recorded for 26 subjects and was 8.4 weeks (SD 14.5). Thirty-nine subjects (69%) received total parenteral nutrition for ≥2 weeks. Age ≤12 months old was more common among subjects with multiple fractures (Table 1). Subjects with multiple fractures were hospitalized for a longer period postfracture (mean 128 vs 73 days, $P = .17$), although this difference was not statistically significant.

Preterm infants

Twenty-six subjects were born preterm (gestational age < 37 weeks) at a mean of 30.0 (SD 4.5) weeks, with mean birth weight of 1258 g (SD 815; Supplementary Table 2). Among the 26 preterm infants, 92% had fractures detected by 12 months' corrected age, and all had fractures detected by 24 months corrected age. Mean chronologic age at the time of index fracture was 6.0 months for preterm children (3.8 months

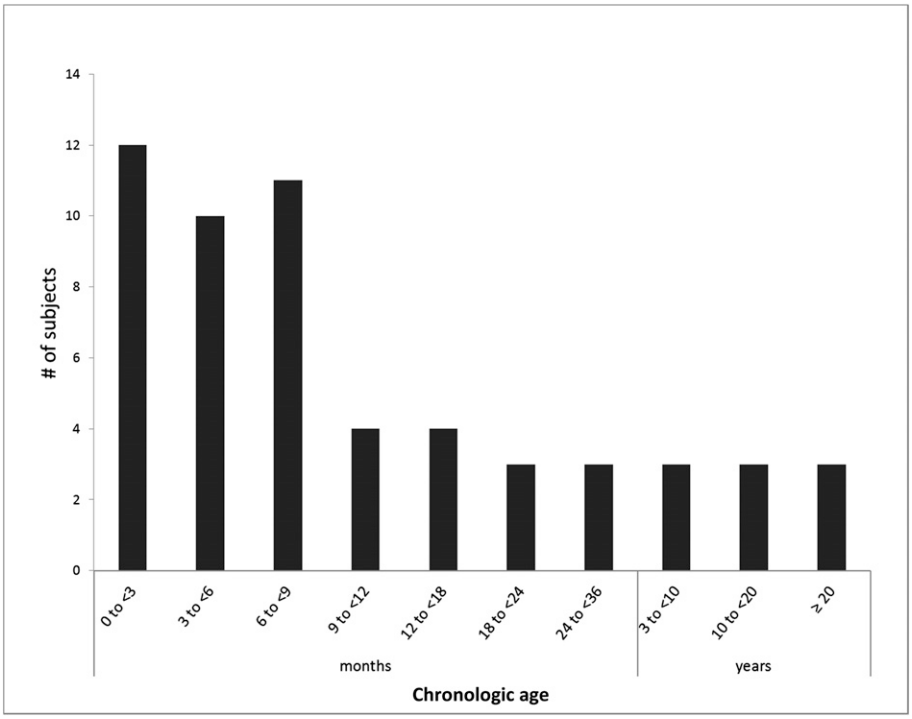

FIGURE 2 Chronologic age at time of index fracture in 56 subjects.

corrected for gestational age), compared with 25.2 months for term children ($P = .03$). Preterm children sustained 59 of the 99 (59.6%) index fractures, and 26 of the 29 (89.7%) additional fractures sustained after index fracture. Compared with subjects born at term, those born preterm had a higher number of fractures (mean 3.3 vs 1.6, $P = .01$). Preterm children sustained the majority of rib (17 of 22), radius (6 of 8), ulna (7 of 8), and spine (4 of 5) fractures, and all 7 fibular fractures. Preterm children had longer duration of mechanical ventilation and parenteral nutrition therapy. There were no differences in diuretic or glucocorticoid use between the preterm and term children. More preterm children had weight-for-age *z* score less than or equal to –2 (68.2% vs 30.8%, $P = .01$) and length-for-age *z* score less than or equal to –2 (61.9% vs 42.9%, $P = .27$) within 60 days of the index fracture. Among preterm children, other admission diagnoses included congenital heart disease ($n = 5$, 19%), esophageal atresia ($n = 6$, 23.1%), transplant ($n = 1$, 3.9%), and other ($n = 2$, 7.7%). Mortality was similar among preterm and term children (30.8% vs 26.1%, $P = .72$).

Laboratory Values

Calcium and phosphorus were measured before fracture in 49 subjects, with a mean calcium value of 9.6 mg/dL (2.4 mmol/L; SD 1.0, range 5.5–11.1 mg/dL) and a mean phosphorus value of 4.9 mg/dL (1.6 mmol/L; SD 1.3, range 1.5–8.3 mg/dL). Among 46 subjects with serum 25OHD levels measured (mean 32.9 ng/mL [82.1 mmol/L], SD 16.1), 25OHD levels revealed deficiency (<20 ng/mL [<50 mmol/L]) in 8, 20 to ≤30 ng/mL (50 to ≤75 mmol/L) in 11, and sufficiency (≥30 ng/mL [75 mmol/L]) in 27 subjects. Mean TSH was 4.4 uU/mL (SD 5.0) in 34 subjects. Three subjects had an elevated TSH (range 6.6–28.4 uU/mL) with normal or low thyroxine. No subjects had primary hyperthyroidism.

Mode of Detection and Survival Status

Thirty-two (57%) subjects had 69 (54%) fractures reported through SERS (Supplementary Table 3). Among the 32 SERS-identified subjects, fractures were detected as an incidental finding in 50.0%, due to complaint of pain in 34.4%, limited use/mobility in 9.4%, and witnessed trauma/injury in 6.3%. Among the 24 i2b2-identified subjects, fractures were detected as an incidental finding in 75.0%, due to pain complaint in 20.8% and limited use/mobility in 4.2%. i2b2-identified subjects were more likely to be born preterm (29.2 vs 15.6%) and a lower proportion had esophageal atresia (16.7 vs 31.3%). The proportion of other admission diagnoses was similar in both groups. All i2b2-identified subjects were located in an ICU, whereas 6 SERS-identified subjects were on a non-ICU ward. As of June 2014, 16 (29%) subjects had died (Table 1). Four of 16 (25%) subjects who died had fractures reported through SERS compared with 28 of 40 (70%) surviving subjects ($P = .002$). Mean duration between index fracture and death was 106 days (SD 93). In 10 subjects, cause of death was withdrawal of care during the hospitalization that included the index fracture. Among subjects who died, primary diagnoses included CHD ($n = 9$), prematurity ($n = 2$), and lung or bone marrow transplant ($n = 2$) and 1 each of epidermolysis bullosa, neurodegenerative disease, and chromosome 4 deletion. All 14 subjects with esophageal atresia survived. Compared with surviving subjects,

TABLE 1 Characteristics of 56 Subjects Who Sustained 128 Fractures During Hospitalization, Mean (SD) or *n* (%)

Patient Characteristic	*n*	Total (*n* = 56)	Single Fracture (*n* = 29)	Multiple Fractures (*n* = 27)	*P*
Age at time of index fracture,[a] *n* (%)	56				.02
Birth–12 mo		37 (66)	15 (52)	22 (81)	
>12 mo		19 (34)	14 (48)	5 (19)	
Gender, *n* (%)	56				.98
Male		25 (45)	13 (45)	12 (44)	
Female		31 (55)	16 (55)	15 (56)	
Admission diagnosis, *n* (%)	56				.24
CHD		13 (23)	8 (28)	5 (19)	
Prematurity		12 (21)	3 (10)	9 (33)	
Esophageal atresia		14 (25)	8 (28)	6 (22)	
Organ or bone marrow transplant		5 (9)	2 (7)	3 (11)	
Other		12 (21)	8 (28)	4 (15)	
GA at birth, *n* (%)	49				.12
Term (≥37 wk)		23 (47)	13 (59)	10 (37)	
<37 wk		26 (53)	9 (41)	17 (63)	
GA, wk	43	33.4 (5.5)	34.8 (4.7)	32.3 (5.8)	.14
Birth wt, g	36	2073 (1215)	2418 (1111)	1764 (1250)	.11
Birth wt for GA *z* score	36	−0.55 (1.1)	−0.34 (1.2)	−0.73 (1.0)	.30
Hospital location, *n* (%)	56				.11
NICU		20 (36)	6 (21)	14 (52)	
Medical-surgical ICU		18 (32)	11 (40)	7 (26)	
Cardiac ICU		12 (21)	8 (28)	4 (15)	
Other		6 (11)	4 (14)	2 (7)	
Acute immobilization, *n* (%)	56				.20
Intubated and/or paralyzed		49 (88)	25 (86)	24 (89)	
Not intubated or paralyzed		7 (12)	4 (14)	3 (11)	
Duration of mechanical ventilation, *n* (%)	56				.46[c]
None		7 (13)	3 (10)	4 (15)	
<4 wk		15 (27)	11 (38)	4 (15)	
4–12 wk		19 (34)	8 (28)	11 (41)	
>12 wk		15 (27)	7 (24)	8 (30)	
Reason fracture suspected, *n* (%)	55				.33
Incidental finding on radiograph		34 (61)	15 (52)	19 (70)	
Pain complaint		16 (29)	10 (34)	6 (22)	
Limited use/mobility		4 (7)	2 (7)	2 (7)	
Witnessed trauma/injury		2 (4)	2 (7)	0 (0)	
Wt for age *z* score,[b] units	52	−2.0 (1.8)	−1.6 (2.1)	−2.4 (1.5)	.11
Wt for age *z* score,[b] *n* (%)	52				.41
z score > −2.0		25 (48)	14 (54)	11 (42)	
z score ≤ −2.0		27 (52)	12 (46)	15 (58)	
Height for age *z* score,[b] units	37	−2.2 (2.1)	−1.8 (2.5)	−2.5 (1.7)	.33
Height for age *z* score,[b] *n* (%)	37				.89
z score > −2.0		18 (49)	8 (50)	10 (48)	
z score ≤ −2.0		19 (51)	8 (50)	11 (52)	
Survival status, *n* (%)	56				.67
Died		16 (29)	9 (31)	7 (26)	
Survived		40 (71)	20 (69)	20 (74)	

P values from *t* test or χ^2 unless otherwise noted. Percentages rounded to nearest whole number. GA, gestational age.

[a] Age corrected for gestational age, if gestational age <37 wk and corrected age <24 mo.

[b] Wt for age and height for age *z* scores obtained within 60 d of index fracture.

[c] *P* values from Mantel-Haenszel χ^2.

subjects who died had a lower weight-for-age *z* score (mean –3.1 vs –1.7, $P = .01$) and height-for-age *z* score (mean –4.0 vs –2.0, $P = .02$).

DISCUSSION

We report a detailed review of fractures detected among hospitalized patients in a tertiary-care children's hospital. These data are novel because most previous pediatric studies examining fracture risk have focused on ambulatory or disease-specific groups. Over 54 months, 56 inpatients sustained 128 fractures, predominantly in long bones, during a single hospitalization. Common characteristics of subjects included immobilization, critical illness, and preterm birth. A voluntary reporting system was insufficient to detect all fractures.

In our study, critically ill, mechanically ventilated infants under 1 year of age sustained the majority of fractures occurring during hospitalization. Immobilization is associated with bone loss within weeks of musculoskeletal disuse that can persist for months[11] and may be a major risk factor for fractures in this population. The predominance of long bone fractures, which comprised 74% of all fractures, may reflect a high severity of illness and immobilization. The femur was the most common fracture site, and 52 (41%) of fractures occurred in the lower extremity. The femur is a weight-bearing bone comprised primarily of cortical bone and should have a rigid cortex that is resistant to fracture. Lower-extremity fractures may be a stronger indicator of poor bone health than those occurring in the upper extremity.[12] The 29% mortality rate in our study also suggests a high severity of illness in some subjects. In studies of adults, the increased mortality observed after a major fracture is largely explained by poor overall health, with a possible contribution from fracture complications.[13,14] We found that mortality varied by primary diagnosis. The high mortality rate among subjects with CHD (69%) contrasted with the low mortality rate among subjects admitted for esophageal atresia repair (0%), who are often relatively healthy. Longitudinal pediatric studies are needed to investigate relationships among severity of illness, fractures, and mortality.

Exposures affecting bone health in critically ill children include loop diuretics,[15,16] parenteral nutrition,[1] and glucocorticoids,[17] all of which were commonly used in our subjects. Less frequent exposures included heparin or low molecular weight heparin use.[18,19] Vitamin D deficiency (25OHD $<$20 ng/mL) was present in 17.1% of 46 subjects with 25OHD levels, a prevalence lower than previously reported in critically ill children at our institution (40%),[20] but similar to ambulatory Boston-area children (12%–42%).[21,22] The high frequency of vitamin D sufficiency may reflect previous treatment of vitamin D insufficiency or use of parenteral nutrition.

Our findings support other data showing that preterm infants commonly sustain long bone and rib fractures while hospitalized.[23,24] Risk factors for metabolic bone disease in preterm infants include low mineral stores at birth,[25] limitations in parenteral calcium and phosphorus delivery, low birth weight, prolonged immobilization, and use of diuretics and glucocorticoids.[26] Compared with term infants, preterm infants sustained more fractures and at a younger age. This finding could reflect a higher frequency of radiographs among preterm versus term infants. However, most subjects were critically ill and underwent multiple radiographs. Additional studies are needed to explore these relationships in further detail.

Our data suggest that fractures are an adverse event that should be systematically tracked during hospitalization. We found that a voluntary reporting system identified 54% of 128 fractures, which appears higher than estimated adverse event voluntary reporting rates of 10% to 20%.[3,4] Our relatively high voluntary reporting rate may reflect the multiyear, interdisciplinary hospital-wide education regarding inpatient fracture identification. Alternatively, the high voluntary reporting rate could reflect incomplete identification of all fractures that occurred during the time frame of the study. Subjects who died were less likely than survivors to have had SERS-identified fractures, and all of the non-ICU-located subjects' fractures were reported through SERS. It is possible that i2b2-reported subjects may have had higher severity of illness that diminished provider attentiveness to SERS reporting.

One method of systematically identifying adverse events is through the use of a trigger tool, which is designed to aid providers by identifying global harm in the hospital setting. Increased awareness of problems that should be addressed allows development of strategies to reduce harm by prevention, mitigation, or research into novel treatments.[5] Our data suggest that the term "fracture" should be considered for inclusion in a global pediatric or ICU-specific trigger tool, to increase recognition of fractures during hospitalization. Recognition of increased fracture risk may lead to further screening and research into novel therapies. The 48% prevalence of multiple fractures and the asymptomatic nature of many fractures suggest that clinicians could consider further evaluation, including a skeletal survey, in critically ill hospitalized patients with 1 identified fracture. Clinicians should consider the reduction or elimination of medications known to contribute to fracture risk. Measures of bone density or markers of bone resorption repeated at intervals during immobilization may help elucidate the natural history of bone loss. Interventions to reduce immobility, including physical therapy, should be studied to determine their impact on fracture risk. For children with fractures during hospitalization, particularly those with lower-extremity fractures,[27] discharge plans should include follow-up bone/mineral evaluations and guidance to optimize bone health.

Our study has several limitations. As a descriptive study, it did not include a control group; identification of appropriate controls was challenging because of varying ages, gestational ages, and underlying diagnoses. The identified fractures likely represent an underestimate of the total number of fractures over the study time period because our search methods likely missed some fractures, and use of the term "portable" may have biased our sample toward detection of fractures among

critically ill children. However, use of 2 complementary methods maximized fracture detection. Another study limitation is that we were not able to determine the exact timing of fractures. Our data suggest that the majority of detected fractures were likely acquired as inpatients, but some detected fractures may have been acquired before hospitalization. Our findings regarding preterm infants may not be generalizable to all NICUs because our NICU population has a high percentage of surgical patients and our hospital is not a birth hospital. The small study size limited power to detect associations and increased likelihood of false-positive associations. Future, prospective studies with control groups and research-standard data collection are needed to confirm our findings and will allow for improved identification of risk factors for fractures during hospitalization.

CONCLUSIONS

Critically ill, immobilized infants under a year of age and often born preterm sustained the majority of fractures occurring during hospitalization. Specific diagnoses such as CHD and esophageal atresia were common. The femur was the most frequently identified fracture site, followed by the humerus. A voluntary reporting system detected 54% of fractures. Fracture should be considered for inclusion in global or ICU-specific trigger tools. Future studies should explore optimal fracture detection strategies, as well as the relationship between fractures, severity of illness, and mortality in children.

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