

Hospital charges and length of stay associated with septicemia among children hospitalized for leukemia treatment in the United States

Veerajalandhar Allareddy, Sankeerth Rampa, Veerasathpurush Allareddy

Boston, USA

Background: This study examines hospital charges and length of stay (LOS) associated with septicemia during hospitalization for leukemia treatment among children aged ≤ 18 years.

Methods: Nationwide Inpatient Sample (year 2008) was used. All hospitalizations (regardless of their discharge status following hospitalization) among children aged ≤ 18 years with a primary diagnosis of leukemia were selected. Leukemia was identified using ICD-9-CM codes in the primary diagnosis field. The presence of septicemia during hospitalization was identified using ICD-9-CM codes in the secondary diagnosis field. Multivariable linear regression analyses were made to examine the effect of septicemia on hospitalization charges and LOS.

Results: Totally 6220 hospitalizations were attributed to leukemia treatment. Among these, 787 had septicemia. The mean hospitalization charge for those with septicemia was \$279 137 and for those without septicemia was \$113 530. The average LOS for those with septicemia was 33.18 days while the LOS for those without septicemia was 13.79 days. Septicemia was associated with increased hospitalization charges and a prolonged duration of stay in hospital after adjustments for confounders ($P < 0.0001$).

Conclusions: Septicemia is associated with adverse outcomes among children hospitalized for leukemia treatment.

World J Pediatr 2012;8(3):222-228

Key words: health outcomes; leukemia; pediatric oncology; septicemia

Introduction

Leukemia is the second leading cause of death accounting for a substantial proportion of all deaths in the United States.^[1] Leukemia is one of the leading causes of death due to disease among children aged between 1 and 14 years.^[1-3] Among children aged 14 years and less, the incidence rate of cancer and mortality rates per 100 000 population was 14.8 and 2.5 in 2004.^[1-3] The last few decades have witnessed an increasing trend towards 5-year higher survival rates in children with cancer.^[1-3] While intensive and aggressive treatment regimens such as chemotherapy, radiation therapy, and surgery have improved the survival of leukemia patients substantially, these regimens can cause immuno-suppression and place the patients at a higher risk for developing infections, septicemia, and related complications.^[4-7] It has been reported that a high proportion of pediatric patients with sepsis have leukemia.^[8] Watson et al^[9] reported that among children hospitalized with severe sepsis, about 23% of the children aged 10-14 years and 14% of those aged 15-19 years had neoplastic disorders. Among all childhood cancers, leukemia is the most prevalent.

There is a paucity of nationally representative data on the occurrence and impact of septicemia on outcomes in pediatric patients hospitalized for leukemia treatment using nationally representative samples. The objective of the current study is to examine outcomes including hospital charges and length of stay associated with septicemia during hospitalization for leukemia treatment among patients aged 18 years and younger in the United States. We hypothesized that occurrence of septicemia is associated with a substantial utilization of hospital resources and will be reflected as higher hospital charges and a prolonged duration of stay in hospital.

Author Affiliations: Department of Pediatric Critical Care and Pharmacology, Rainbow Babies and Children's Hospital, University Hospitals, Case Medical Center, USA (Allareddy V); Nance College of Business Administration, Cleveland State University, Ohio, USA (Rampa S); Department of Developmental Biology, Harvard School of Dental Medicine, USA (Allareddy V)

Corresponding Author: Veerasathpurush Allareddy, Department of Developmental Biology, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115, USA (Tel: 216-571-1009; Email: VA15@hsdm.harvard.edu)

doi: 10.1007/s12519-012-0361-5

©Children's Hospital, Zhejiang University School of Medicine, China and Springer-Verlag Berlin Heidelberg 2012. All rights reserved.

Methods

Data sources

We performed retrospective analyses of the Nationwide Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project for the year 2008.^[10] The NIS is the only all-payer inpatient care database for all hospitalizations in the United States and the year 2008 dataset contains data drawn from 42 State Inpatient Databases and includes discharge information on 8 158 381 discharges drawn from 1056 hospitals.^[10-12] Each discharge from the NIS contains a discharge weight which can be used to project all estimates to national levels. The NIS dataset draws its sample from discharges of all community and non-rehabilitation hospitals in the states participating in the Healthcare Cost and Utilization Project. The NIS dataset provides information on nearly 100 variables related to patients including age, gender, race, insurance status, primary and secondary diagnoses, procedures performed during hospitalization, hospital charges, length of stay, discharge status, type of admission, and hospital characteristics (such as geographic region of hospital, location of hospital, teaching status of hospital, bed size, and children specialty status).^[10]

Patient selection

All hospitalizations of patients aged 18 years and less with primary diagnosis codes for any leukemias were selected for analysis. ICD-9-CM codes were used to identify discharges that were hospitalized primarily for leukemia treatment. The ICD-9-CM codes selected included those for lymphoid leukemia (204.xx), myeloid leukemia (205.xx), monocytic leukemia (206.xx), other specified leukemia (207.xx), and leukemia of unspecified type (208.xx). The NIS data have information on 15 diagnosis codes. Cases of septicemia were identified using the Clinical Classification Software code "2" in the secondary diagnosis fields.^[10]

Outcomes

Hospital charges (in \$) and length of stay (in days) were the main outcome variables of interest. Information on these variables was obtained from the NIS dataset. Hospital charges refer to the charges that the hospital levied to the patients and not the cost of care provided to patients or the amount reimbursed for the services rendered and all hospital charges are in year 2008 dollars. The length of stay refers to the number of days a patient was hospitalized during the index hospitalization.

Independent variables

The primary independent variable was the presence of septicemia during the index hospitalization. Other

independent variables that were available in the NIS dataset and were examined in the current study included age, gender, type of leukemia, discharge status, type of admission, presence of co-morbid conditions,^[13] insurance status, teaching status of hospital, location of hospital, hospital bed size, and geographic region of hospital. Age was used as a continuous variable while all other variables were used as categorical variables.

Analytical approach

Descriptive statistics was used to describe the baseline characteristics of the patients who were hospitalized primarily for leukemia treatment. To examine the association between septicemia and outcomes including length of stay (LOS) in hospital and total hospitalization charges, multivariable linear regression approach was used. Since hospital charge and LOS data were highly skewed, these were log transformed and were used as the dependent variables in the multivariable linear regression analysis. Separate models were used for hospital charges and LOS. Potential confounding factors including age (each 1 year increase), gender (male is reference), disposition of patient (died in hospital is reference), insurance status (private insurance is reference), type of leukemia, type of admission (non-elective is reference), presence of co-morbid conditions, teaching status of hospital (non-teaching hospital is reference), location of hospital (rural location is reference), geographic region (south is reference), and hospital bed size (small or medium bed size is reference) were adjusted in the multivariable linear regression models. For identifying co-morbid conditions, the method of Elixhauser et al^[13] was used. Twenty-nine co-morbid conditions were identified from the NIS dataset, and simple linear regression analyses were conducted to examine the independent association of each of the 29 co-morbid conditions on hospital charges and LOS. All co-morbid conditions that were statistically significant in the simple regression models at $P < 0.05$ were included in the final multivariable linear regression models. With regards to type of leukemia, as mentioned earlier, ICD-9-CM codes were used to identify the discharges. Since the number of individual leukemia discharges under the different ICD-9-CM codes tended to be very low in numbers, some of the ICD-9-CM codes were combined into one group and used as the reference variable in the multivariable regression models.

All multivariable linear regression analyses were conducted using SAS callable SUDAAN and variances were computed by the Taylor Linearization Method using a "With Replacement" design. The stratification unit was used as the NIS hospital stratum and each individual hospitalization was the unit of analysis. The discharge weight variable assigned to each discharge

was used to project to national estimates. The effects of clustering of outcomes within hospitals were adjusted in all regression models. All of the statistical tests were 2-sided, and a *P* value less than 0.05 was considered to be statistically significant. All analyses were performed using Statistical Analysis Systems Software, version 9.2 (SAS Institute, Cary, NC), and SUDAAN Version 10.0.1 (Research Triangle Park, NC) software.

Results

In this sample, a total of 6220 hospitalizations were attributed primarily to leukemia treatment among children. The characteristics of hospitalized patients are summarized in Tables 1 and 2. The average age of

the hospitalized patients was 7.7 years and 57% of the hospitalizations occurred in males. The most frequently presenting primary diagnosis was acute lymphoid leukemia, without mention of having achieved remission or failed remission (*n*=4110 hospitalizations), followed by acute myeloid leukemia, without mention of having achieved remission or failed remission (*n*=990 hospitalizations) (Table 2).

The overall in-hospital mortality rate was 3.4% (209 patients died in hospitals) (Table 1). A total of 787 hospitalizations (12.7%) had septicemia. Close to 78% of all hospitalizations were discharged routinely while 15% were discharged to home health care. Private insurance plans were the primary payers for 53% of all hospitalizations and Medicaid covered 41.5%

Table 1. Characteristics of patients hospitalized for leukemia treatment

Characteristics	Frequency (%)
Sex	
Male	3544 (57.2)
Female	2650 (42.8)
Missing data	26
Discharge status	
Routine	4835 (77.7)
Transfer to another short term hospital	199 (3.2)
Other transfers (skilled nursing facility, intermediate care facility, and another type of facility) or discharged against medical advice	56 (0.9)
Home health care	921 (14.8)
Died	209 (3.4)
Insurance status	
Medicare	15 (0.2)
Medicaid	2582 (41.5)
Private insurance	3296 (53.0)
Self pay/no charge	120 (1.9)
Others	202 (3.2)
Missing data	5
Type of admission	
Elective	1666 (26.8)
Non-elective	4543 (73.2)
Missing data	11
Hospital teaching status	
Teaching	5290 (85.0)
Non-teaching	930 (15.0)
Missing data	0
Hospital bed size	
Small	474 (7.6)
Medium	1195 (19.2)
Large	4551 (73.2)
Missing data	0
Hospital location	
Rural	68 (1.1)
Urban	6152 (98.9)
Missing data	0
Hospital region	
Northeast	1210 (19.5)
Midwest	918 (14.8)
South	2197 (35.3)
West	1895 (30.5)
Missing	0

Table 2. Type of leukemia for which patients were hospitalized

ICD-9-CM code	Type of leukemia	Frequency (%)
204.00	Acute lymphoblastic leukemia – without mention of having achieved remission / failed remission	4110 (66.1)
204.01	Acute lymphoblastic leukemia – in remission	500 (8.0)
204.02	Acute lymphoblastic leukemia – in relapse	59 (0.9)
204.10	Chronic lymphoblastic leukemia – without mention of having achieved remission / failed remission	DS
204.81	Other lymphoblastic leukemia – in remission	DS
205.00	Acute myeloid leukemia – without mention of having achieved remission / failed remission	990 (15.9)
205.01	Acute myeloid leukemia – in remission	137 (2.2)
205.02	Acute myeloid leukemia – in relapse	46 (0.7)
205.10	Chronic myeloid leukemia – without mention of having achieved remission / failed remission	145 (2.3)
205.11	Chronic myeloid leukemia – in remission	DS
205.12	Chronic myeloid leukemia – in relapse	DS
205.30	Myeloid sarcoma – without mention of having achieved remission / failed remission	19 (0.3)
205.80	Other myeloid leukemia – without mention of having achieved remission / failed remission	DS
205.90	Unspecified myeloid leukemia – without mention of having achieved remission / failed remission	20 (0.3)
206.02	Acute monocytic leukemia – in relapse	DS
206.80	Other monocytic leukemia – without mention of having achieved remission / failed remission	DS
207.00	Acute erythremia and erythroleukemia – without mention of having achieved remission / failed remission	DS
207.80	Other specified leukemia – without mention of having achieved remission / failed remission	30 (0.5)
208.00	Acute leukemia of unspecified type – without mention of having achieved remission / failed remission	69 (1.1)
208.01	Acute leukemia of unspecified type – in remission	DS
208.90	Unspecified leukemia – without mention of having achieved remission / failed remission	39 (0.6)

ICD-9-CM codes for several leukemias that had a cell count of "0" are not presented in this table. DS: discharge information suppressed (Individual cell counts for this data are ≤ 10 . HCUP data user agreement precludes us from presenting these estimates. Hence these were combined into one group and presented).

Table 3. Hospitalization charges, and length of stay of patients hospitalized for leukemia treatment

Characteristics	Mean (standard error)	Total US hospitalization charges/length of stay
Total hospital charges	\$134 346 (15 074)	\$787 889 554
Length of stay	16.24 d (1.56)	101 034

of all hospitalizations. About 73% of all admissions occurred on a non-elective basis (emergency or urgent admissions). Most of the hospitalizations occurred among the urban and large bed size hospitals.

The mean total hospitalization charges and LOS were \$134 346 and 16.24 days respectively (Table 3). The total hospitalization charge across the entire United States was close to \$788 million and total hospitalization days were 101 034. The mean hospitalization charge for those with septicemia was \$279 137 while the charges for those without septicemia were \$113 530. The average LOS for those with septicemia was 33.18 days while the LOS for those without septicemia was 13.79 days.

The results of the multivariable linear regression analyses examining the association between the independent variables and hospital charges are summarized in Table 4. The presence of septicemia was associated with increased hospitalization charges even after adjusting for several other possible confounding factors (Beta coefficient = 0.6929, 95% CI = 0.4992–0.8867, $P < 0.0001$). The estimated increase in hospitalization charges associated with septicemia was \$134 279 after controlling of confounding factors. Other independent variables that were associated with increased hospitalization charges were elective admission ($P = 0.04$), congestive heart failure ($P = 0.02$), coagulopathy ($P = 0.0009$), hypertension ($P < 0.0001$), fluid and electrolyte disorders ($P < 0.0001$), paralysis ($P = 0.01$), peripheral vascular disorders ($P = 0.048$), pulmonary circulation disorders ($P = 0.0001$), urban hospital ($P = 0.0002$), and teaching hospitals ($P = 0.0007$).

The results of the multivariable linear regression analyses examining the association between the independent variables and LOS are summarized in Table 5. The presence of septicemia was associated with increased hospitalization charges (Beta coefficient = 0.6295, 95% CI = 0.4574–0.8015, $P < 0.0001$). The estimated increase in LOS associated with septicemia was 14.24 days after adjusting for confounders. Other independent variables that were associated with increased LOS were female gender ($P = 0.006$), congestive heart failure ($P = 0.04$), coagulopathy ($P = 0.0006$), hypertension ($P < 0.0001$), fluid and electrolyte disorders ($P < 0.0001$), pulmonary circulation disorders ($P < 0.0001$), urban hospital ($P = 0.01$), and teaching hospitals ($P = 0.004$).

Table 4. Factors associated with hospital charges* (multivariable linear regression analysis)

Characteristics	Beta coefficient (95% CI)	P value
Presence of septicemia		
Yes	0.6929 (0.4992 – 0.8867)	<0.0001
No	Reference	
Sex		
Female	0.0570 (-0.0779 – 0.1919)	0.40
Male	Reference	
Primary diagnosis		
204.00	-0.3080 (-0.5159 – -0.1001)	0.004
204.01	-0.5552 (-1.0917 – -0.0187)	0.04
205.00	0.2309 (0.0125 – 0.4492)	0.04
Others	Reference	
Type of admission		
Elective	0.3164 (0.0142 – 0.6185)	0.04
Non-elective	Reference	
Insurance status		
Medicare	0.4363 (-0.6362 – 1.5087)	0.42
Medicaid	-0.0369 (-0.2610 – 0.1873)	0.74
Self pay/no charge	0.2039 (-0.1966 – 0.6044)	0.31
Other insurance plans	-0.2335 (-0.6930 – 0.2260)	0.31
Private insurance	Reference	
Disposition of patient		
Routine discharge	-0.2734 (-0.7194 – 0.1726)	0.22
Transfer to another short term facility	-1.2826 (-1.9828 – -0.5824)	0.0006
Other transfers/Against medical advice	-1.4843 (-2.6916 – -0.2771)	0.02
Home health care	-0.0470 (-0.5968 – 0.5029)	0.86
Died in hospital	Reference	
Presence of co-morbid conditions		
AIDS	-0.5991 (-1.4642 – 0.2661)	0.17
Chronic blood loss anemia	-0.0824 (-0.5367 – 0.3719)	0.72
Congestive heart failure	0.7221 (0.1125 – 1.3316)	0.02
Coagulopathy	0.4810 (0.2074 – 0.7545)	0.0009
Depression	0.0919 (-0.4134 – 0.5973)	0.72
Diabetes – uncomplicated	0.4819 (-0.0567 – 1.0206)	0.08
Hypertension	0.6118 (0.3450 – 0.8787)	<0.0001
Liver disease	0.3215 (-0.0121 – 0.6551)	0.06
Fluid and electrolyte disorders	0.5339 (0.3631 – 0.7048)	<0.0001
Metastatic cancer	-0.4181 (-1.1854 – 0.3491)	0.28
Neurological disorders	0.2188 (-0.1044 – 0.5420)	0.18
Paralysis	0.8258 (0.1612 – 1.4904)	0.01
Peripheral vascular disorders	0.6841 (0.0037 – 1.3644)	0.048
Pulmonary circulation disorders	0.9142 (0.4672 – 1.3613)	0.0001
Weight loss	0.1382 (-0.2592 – 0.5356)	0.49
Age in years (1 year increase)	0.0143 (-0.0044 – 0.0331)	0.13
Location of hospital		
Urban	2.2117 (1.1023 – 3.3211)	0.0002
Rural	Reference	
Teaching status of hospital		
Teaching	0.6344 (0.2785 – 0.9902)	0.0007
Non-teaching	Reference	
Geographic region of hospital		
Northeast	0.3513 (-0.0391 – 0.7416)	0.08
Midwest	-0.0670 (-0.4117 – 0.2777)	0.70
West	0.5409 (-0.0213 – 1.1031)	0.06
South	Reference	
Hospital bed size		
Large	-0.0660 (-0.4793 – 0.3473)	0.75
Small/medium	Reference	

*: Outcome variable is log transformed hospital charges. Positive estimates indicate increased hospital charges compared to reference while negative estimates indicate decreased hospital charges compared to reference. AIDS: acquired immune deficiency syndrome.

Table 5. Factors associated with length of stay in hospital* (multivariable linear regression analysis)

Characteristics	Beta coefficient (95% CI)	P value
Presence of septicemia		
Yes	0.6295 (0.4574 – 0.8015)	<0.0001
No	Reference	
Sex		
Female	0.1766 (0.0530 – 0.3003)	0.006
Male	Reference	
Primary diagnosis		
204.00	-0.4592 (-0.6175 – -0.3008)	<0.0001
204.01	-0.4536 (-0.8790 – 0.0281)	0.04
205.00	0.2826 (0.0787 – 0.4866)	0.01
Others	Reference	
Type of admission		
Elective	0.1409 (-0.0611 – 0.3430)	0.17
Non-elective	Reference	
Insurance status		
Medicare	0.4495 (-0.2123 – 1.1113)	0.18
Medicaid	0.0123 (-0.1332 – 0.1579)	0.87
Self pay/no charge	0.1507 (-0.1020 – 0.4035)	0.24
Other insurance plans	-0.1410 (-0.4332 – 0.1512)	0.34
Private insurance	Reference	
Disposition of patient		
Routine discharge	-0.2926 (-0.7728 – 0.1877)	0.23
Transfer to another short term facility	-1.2763 (-1.9120 – -0.6406)	0.0002
Other transfers/Against medical advice	-0.1029 (-1.0711 – 0.8653)	0.83
Home health care	-0.0488 (-0.5675 – 0.4698)	0.85
Died in hospital	Reference	
Presence of co-morbid conditions		
AIDS	-0.0351 (-0.5851 – 0.5150)	0.90
Congestive heart failure	0.4746 (0.0212 – 0.9280)	0.04
Chronic pulmonary disease	-0.2824 (-0.6204 – 0.0557)	0.10
Coagulopathy	0.3752 (0.1676 – 0.5828)	0.0006
Depression	0.3437 (-0.1314 – 0.8189)	0.15
Diabetes – uncomplicated	0.1681 (-0.2046 – 0.5409)	0.37
Hypertension	0.4596 (0.2785 – 0.6407)	<0.0001
Fluid and electrolyte disorders	0.4406 (0.3087 – 0.5725)	<0.0001
Metastatic cancer	-0.7678 (-1.6013 – 0.0657)	0.07
Neurological disorders	0.1958 (-0.0594 – 0.4509)	0.13
Paralysis	0.2227 (-0.5448 – 0.9902)	0.56
Peripheral vascular disorders	0.3037 (-0.2368 – 0.8442)	0.26
Pulmonary circulation disorders	0.8727 (0.5213 – 1.2241)	<0.0001
Solid tumor without metastasis	0.1798 (-0.3101 – 0.6697)	0.46
Weight loss	0.2611 (-0.0718 – 0.5940)	0.12
Age in years (1 year increase)	-0.0009 (-0.0143 – 0.0126)	0.90
Location of hospital		
Urban	1.1439 (0.2502 – 2.0375)	0.01
Rural	Reference	
Teaching status of hospital		
Teaching	0.4095 (0.1344 – 0.6845)	0.004
Non-teaching	Reference	
Geographic region of hospital		
Northeast	0.1894 (-0.0901 – 0.4689)	0.18
Midwest	-0.1627 (-0.4019 – 0.0765)	0.18
West	0.0943 (-0.1796 – 0.3682)	0.49
South	Reference	
Hospital bed size		
Large	-0.0417 (-0.3228 – 0.2394)	0.77
Small/medium	Reference	

*: Outcome variable is log transformed length of stay in hospital. Positive estimates indicate increased length of stay compared to reference while negative estimates indicate decreased length of stay compared to reference. AIDS: acquired immune deficiency syndrome.

Discussion

While it is acknowledged that patients with cancers are more prone to developing infectious complications and consequently suffer from poor outcomes, there are very few studies that actually document the same using samples of hospitalizations that are nationally representative.^[5,6,8,9] Several studies have shown that the development of sepsis in pediatric cancer patients is associated with poor prognosis and the results of our study further lend credence to this.^[5,14-16] The results of our study are drawn from the largest hospital discharge dataset for children drawn from different types of hospitals across the United States.^[10] The results are thus more generalizable and may accurately portray the current scenario with regards to the incidence of septicemia and adverse outcomes associated with its occurrence among hospitalized pediatric patients undergoing leukemia treatment.

The results of our study indicate that hospitalizations with septicemia associated with an average of \$134 279 in excess hospital charges and 14.24 extra days in the hospital even after adjustment for all confounding factors that were available from the NIS dataset. All these indicate the adverse outcomes associated with septicemia during hospitalization. Approximately 13% of cases of all leukemia-related hospitalizations in this dataset had septicemia. If we were to impute the adverse outcomes to the entire complement of cases of septicemia in this dataset, it is evident that septicemia is associated with substantial utilization of resources. Several studies have shown that sepsis is a major cause of mortality in hospitalized patients^[17-19] and about \$17 billion is spent annually on its treatment.^[18] Williams et al^[20] reported national estimates for cancer patients with severe sepsis in 1999 and attributed 8.5% of all cancer deaths to septicemia. Septicemia was the tenth leading cause of death in the United States in 2005 and 34 136 deaths were due to septicemia.^[1]

It is critically important that future studies should identify risk factors contributing to the development of septicemia during leukemia-related hospitalizations. The results of our study further underscore the importance of implementing quality improvement initiatives targeting this subset of population that are at a higher risk of developing septicemia. Aggressive and timely preventive and intervention strategies for this cohort of patients who are at a higher risk of developing septicemia could substantially improve clinical and economic outcomes. The potential increase in LOS could be due to infections that result from treatment-associated immunosuppression, although the improvement of survival is linked to more aggressive cancer treatment regimens.^[20-22] Respiratory failure (especially early acute respiratory distress syndrome)

in addition to severe sepsis is a known major risk factor for cancer-related Intensive Care Unit (ICU) mortality and increased LOS. Other factors that may contribute to increase in LOS include non-initiation of early non-invasive positive pressure ventilation in immunocompromised children with early ARDS and the complications associated with a prolonged positive pressure ventilation. The need for sedative drug withdrawal monitoring can independently prolong the ICU LOS. The widespread use of vasoactive agents in settings without appropriate hemodynamic monitoring and the lack of protocols for timely identification of sepsis leading to severe sepsis/shock can delay early pediatric ICU referral with subsequent increase in the length of hospital stay due to potentially avoidable complications from septicemia. Likewise, the lack of an ICU team specialized to assess early multi-organ failure signs triggering early ICU admission and treatment may contribute to increased LOS. Lack of well-established clinical guidelines or inadequate implementation of existing clinical guidelines for management of septicemia in immunocompromised children with cancer in the ICU can lead to increased LOS and ICU mortality.

The demonstration of extensive resource utilization in terms of LOS and hospital charges for the immunocompromised children emphasizes the need for implementation of potential strategies that maximizes such outcomes as aggressive preventive care, early diagnosis of septicemia, risk stratification, judicious, timely and cost-effective use of anti-infective agents and equipment, institutionalized disease specific protocols designed to limit complications, and the need for advances in cancer-related critical care practice and sepsis therapy.

Our study is a retrospective analysis of hospital discharge data and consequently the results of the study and the conclusions drawn from them should be viewed while considering several limitations. Our study quantifies the incremental excess hospital charges and the length of hospital stay that is associated with sepsis during treatment for leukemia hospitalizations among children. The actual cause and effect relationship between sepsis and the outcomes of interest cannot be proved by this retrospective study. One of the outcome variables of interest was the hospital charge. It is likely that the actual costs incurred by the hospitals to treat sepsis are different from the charges levied to the patients. While the dataset provides information on the presence of sepsis during hospitalization, there is no information on the severity of sepsis. It is reasonable to expect that more severe sepsis requires more resource utilization and consequently a more prolonged length of stay in hospital and higher hospital charges. Variables

such as the Pediatric Risk of Mortality (PRISM) score are not available in this dataset and previous studies have shown that PRISM score is a significant predictor of mortality among pediatric cancer patients with sepsis.^[6] Because of the lack of this information, we were unable to conduct a more thorough risk adjustment for the severity of condition. The NIS dataset does not provide any information on post-hospitalization outcomes and our estimates associated with the occurrence of sepsis reflect the resource utilization only within the hospital setting.^[10] The immediate post-discharge outcomes and the long-term impact of sepsis are not known. The possibility of omitted variable bias should not be discounted as the matching of cases and controls was limited to the variables available in the dataset. There could be a host of patient-related characteristics that could influence outcomes and were not captured in our dataset. For example, we used the method of Elixhauser et al^[13] to assess the co-morbid burden on outcomes during hospitalization. While this algorithm captures the presence of co-morbid conditions that have been shown to influence outcomes, the actual severity of the condition is not known.

In conclusion, our study quantifies the hospital charges, and the length of hospital stay associated with septicemia among patients aged 18 years and less hospitalized for leukemia treatment in the United States in 2008. Septicemia is associated with poor hospitalization outcomes in terms of excess hospital charges and a prolonged length of stay in hospital.

Funding: This study is authors' own work and is not funded by any agency.

Ethical approval: The current study is a secondary data analysis of a publically available dataset available from Agency for Healthcare Research and Quality. A data user agreement was signed with this agency and the data was acquired.

Competing interest: None of the authors listed in this manuscript have any financial or other conflicts of interest associated with publication of this study results.

Contributors: Veerajalalandhar Allareddy contributed to acquiring data, data analysis, writing of manuscript, and final approval of manuscript. Sankeerth Rampa contributed to data analysis, data interpretation, writing of manuscript, and final approval of manuscript. Veerasathpurush Allareddy contributed to study idea, data analysis, data interpretation, writing of manuscript, and final approval of manuscript.

References

- 1 US Mortality data (2005). National Center for Health Statistics, Centers for Disease Control and Prevention. 2008.
- 2 Surveillance, Epidemiology, and End Results Program, 1975-2004. Division of Cancer Control and Population Sciences, National Cancer Institute. 2007.

- 3 American Cancer Society: Cancer Statistics 2008.
- 4 Arceci RJ. Progress and controversies in the treatment of pediatric acute myelogenous leukemia. *Curr Opin Hematol* 2002;9:353-360.
- 5 Ben Abraham R, Toren A, Ono N, Weinbroum AA, Vardi A, Barzilay Z, et al. Predictors of outcome in the pediatric intensive care units of children with malignancies. *J Pediatr Hematol Oncol* 2002;24:23-26.
- 6 Fiser RT, West NK, Bush AJ, Sillos EM, Schmidt JE, Tamburro RF. Outcome of severe sepsis in pediatric oncology patients. *Pediatr Crit Care Med* 2005;6:531-536.
- 7 Pui CH, Campana D, Evans WE. Childhood acute lymphoblastic leukaemia—current status and future perspectives. *Lancet Oncol* 2001;2:597-607.
- 8 Tamburro R. Pediatric cancer patients in clinical trials of sepsis: factors that predispose to sepsis and stratify outcome. *Pediatr Crit Care Med* 2005;6(3 Suppl):S87-91.
- 9 Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J, Angus DC. The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med* 2003;167:695-701.
- 10 HCUP Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP), 2008. Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. <http://www.hcup-us.ahrq.gov/nisoverview.jsp> (accessed November 20, 2010).
- 11 Nationwide Inpatient Sample (NIS) - Description of Data Elements. Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. <http://www.hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp> (accessed November 20, 2010).
- 12 Nationwide Inpatient Sample (NIS) - HCUP Coding Practices. Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. <http://www.hcup-us.ahrq.gov/db/coding.jsp> (accessed November 20, 2010).
- 13 Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8-27.
- 14 Bonig H, Schneider DT, Sprock I, Lemburg P, Gobel U, Nurnberger W. 'Sepsis' and multi-organ failure: predictors of poor outcome after hematopoietic stem cell transplantation in children. *Bone Marrow Transplant* 2000;25 Suppl 2:S32-34.
- 15 Hallahan AR, Shaw PJ, Rowell G, O'Connell A, Schell D, Gillis J. Improved outcomes of children with malignancy admitted to a pediatric intensive care unit. *Crit Care Med* 2000;28:3718-3721.
- 16 van Veen A, Karstens A, van der Hoek AC, Tibboel D, Hahlen K, van der Voort E. The prognosis of oncologic patients in the pediatric intensive care unit. *Intensive Care Med* 1996;22:237-241.
- 17 Alberti C, Brun-Buisson C, Goodman SV, Guidici D, Granton J, Moreno R, et al. Influence of systemic inflammatory response syndrome and sepsis on outcome of critically ill infected patients. *Am J Respir Crit Care Med* 2003;168:77-84.
- 18 Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med* 2001;29:1303-1310.
- 19 Angus DC, Wax RS. Epidemiology of sepsis: an update. *Crit Care Med* 2001;29(7 Suppl):S109-116.
- 20 Williams MD, Braun LA, Cooper LM, Johnston J, Weiss RV, Qualy RL, et al. Hospitalized cancer patients with severe sepsis: analysis of incidence, mortality, and associated costs of care. *Crit Care* 2004;8:R291-298.
- 21 Chanock S. Evolving risk factors for infectious complications of cancer therapy. *Hematol Oncol Clin North Am* 1993;7:771-793.
- 22 Allegretta GJ, Weisman SJ, Altman A. Oncologic emergencies II. Hematologic and infectious complications of cancer and cancer treatment. *Pediatr Clin North Am* 2003;32:613-624.

Received August 1, 2011

Accepted after revision December 7, 2011