Outcomes and Complications of Pediatric Acute Myelogenous Leukemia Treated at Rady Children's Hospital San Diego: a Retrospective Study

Abstract

Background: While overall 5-year survival has improved by approximately 50% in pediatric AML patients in the last twenty years with intensification of antineoplastic therapy and advancement in antimicrobial therapy, treatment-related complications continue to be a major problem. Prior studies have demonstrated that mandatory hospitalization during profound neutropenia did not reduce infections or significantly reduce non-relapse mortality (NRM). The aim of this study was to evaluate the effect of our supportive care measures on treatment-related mortality (TRM), event free survival (EFS), and overall survival (OS). Secondary aims of this study were to document infectious complications of AML therapy, which organisms were isolated most frequently from blood cultures, quantify the number of antibiotic modifications made for each patient throughout treatment and observe how many patients were admitted to the pediatric intensive care unit (PICU) for septic shock and acute respiratory distress syndrome (ARDS).

Methods and Materials: A retrospective chart review of 35 pediatric AML patients treated at Rady Children's Hospital of San Diego (RCHSD) from January 2006 and July 2013 were examined. The OS, EFS and TRM were determine for this cohort and compared to the outcomes of those pediatric AML patients treated under the Children's Oncology Group (COG) AAML0531 and CCG2961.

Results: Of the 35 patients analyzed, the OS for AML patients treated at RCHSD was 75%, EFS was 59% and TRM was calculated as 3%. These values were compared to the OS, EFS and TRM of patients treated on the COG AAML0531 and CCG2961 protocols. Only one individual died from treatment related causes making TRM 3%. Additionally, infectious complications were also examined and among this cohort of patients, bacteremia (46.7%) and diarrhea due to C. difficile (16.5%) were the most common infectious complications throughout treatment. Of the organisms that grew from blood cultures, Streptococcus viridans (22%) and Staphylococcus epidermidis (20%) were the two most common organisms isolated. Vancomycin was the most common antibiotic modification when either of these bacteria were identified. Of those requiring higher level of care for septic shock and ARDS, 12.5% of patients required PICU admissions during induction. 18.8% of patients required PICU level of care throughout the entire course of treatment.

Conclusions: Intensive supportive care protocol for pediatric AML patients treated at RCHSD had a positive effect on OS, EFS and TRM as evidenced by comparisons to children treated on the CCG-2961 and AAML0531 protocols. Also, infectious complications are very common among AML patients during treatment with bacteremia and C. difficile colitis being the most frequently identified throughout course of treatment. Gram-positive organisms were the most commonly bloodstream isolates among bacteremic patients with the addition of vancomycin as the most common antibiotic modification made. Further considerations should include the addition of vancomycin as a prophylactic antibacterial agent and metronidazole as empiric therapy for those with diarrhea, even with unknown causes.

Introduction

Recent studies of pediatric AML patients have shown that overall 5-year survival has increased to about 50% in the last two decades.[2] However, while intensification of antineoplastic therapy and improvements in antimicrobial therapy have improved survival in this patient population, treatment-related complications remain a major problem.

Infection continues to be a major cause of morbidity and mortality in pediatric AML patients.[3] Previous trials studying infectious complications of children with AML noted 29% to 60% had at least one microbiological infection. Infectious complications directly contribute to mortality and prolong hospital stays. Infections also compromise the ability to deliver effective chemotherapy.[4] A number of studies have analyzed the incidence of microbial complications within this patient population. In a retrospective study, 240 children treated at eight Italian medical centers were analyzed for the risk of bacteremia and invasive fungal disease. Bacteremia was

seen in 32% of treatment courses and fungal disease seen in 10%, indicating severe infectious complications occur frequently during treatment of pediatric AML. [5]A retrospective study analyzing 901 children enrolled into the multicenter Acute Myeloid Leukemia-Berlin-Frankfurt-Muenster (AML-BFM) 93 and AML-BFM 98 showed that early diagnosis and appropriate treatment of complications are necessary. The study showed 3.5% of patients died before or during the first fourteen days of treatment. After day 15, the predominant cause of death were complications caused by bacterial and fungal infections.[6] In another retrospective study conducted by Lehrnbecher *et al*, they collected information on the frequency and characteristics of infectious complications among 304 children treated in 30 hospitals according to the multi-institutional clinical trial AML-BFM93. Of the 855 infectious complications that occurred in 304 patients, microbiologically documented infections occurred 275 (32.1%) times. Bloodstream infections occurred in 228 out of the 275 documented microbiological infections. Of the 252 organisms that were isolated, 203 (80.6%) were Gram-positive and 42 (19.4%) were Gram-negative organisms. Diarrhea also developed in 43 patients, and C. difficile was identified in the stool in 26 cases.[7]

In 2006, oncologists at RCHSD instituted an intensive supportive care protocol for pediatric patients undergoing AML therapy. At RCHSD, patients with AML are hospitalized after each course of chemotherapy until the absolute phagocyte count rises for two days and continues to show an upward trend. AML patients must also be deemed clinically stable and afebrile prior to discharge from the hospital. Children are generally discharged after if their absolute neutrophil count (ANC) is at least 200/uL. For the management of febrile neutropenia, empiric antibacterial monotherapy with 4th generation cephalosporin cefepime is initiated in response to a fever (defined as T > 38.3^{o}C) if the patient's ANC is < 500, or < 1000 and expected to decline. Febrile neutropenic AML patients with a cephalosporin allergy or those who require additional anaerobic coverage, such as patients with an obvious gastrointestinal or oral source of infection, instead receive empiric meropenem monotherapy. AML patients with an ANC < 100 are treated with prophylactic antifungals micafungin or voriconazole. AML patients at RCHSD with an ANC < 300 are placed on a low bacteria diet. Other practices include the use of positive pressure and air filters in patient rooms changes in isolation practices. and An initial review of 19 patients treated at RCHSD after the implementation the intensive supportive care protocol was conducted. Among these patients OS was 89% and relapse-free survival (RFS) was 74%. Two of the 19 patients (10%) died due to disease-related reasons. There were no toxic deaths.

In 2013, Sung et al published a report analyzing the effectiveness of supportive care measures to minimize infections among pediatric AML patients. They reported that mandatory hospitalization during profound neutropenia did not reduce infections or significantly reduce non-relapse mortality (NRM). In response to Sung's findings, we set out to evaluate the effect of RCHSD's intensive supportive care measures (specifically, hospitalization through count nadir and recovery, antibacterial monotherapy for empiric treatment of febrile neutropenia, low bacteria diet for AML patients with ANC < 300, and empiric antifungal prophylaxis with voriconazole or micafungin for AML patients with ANC < 100) on treatment-related mortality (TRM), event free survival (EFS), and overall survival (OS) for AML patients diagnosed and treated at RCHSD between Jan 2006 and June 2013. A secondary aim was to document infectious complications of AML therapy at RCHSD during this time period.

Methods and Materials

Trial Description

This retrospective study reviewed and collected data from medical records of 35 de novo AML pediatric patients treated at RCHSD between January 2006 and July 2013 after the institution of the aggressive supportive care protocol. Inclusion criteria were those patients with newly diagnosed AML treated at RCHSD. Exclusion criteria included patients diagnosed with acute promyelocytic leukemia (APML or AML subtype M3). Down Syndrome patients were included although results were analyzed with and without the inclusion of Down

syndrome patients because these patients often receive less intensive therapy because it is well-documented that AML patients with Down Syndrome have a higher incidence of treatment-related toxicities but have an overall better disease response rate than non-Down Syndrome patients. The study was approved by the institutional review board and a waiver of individual HIPPA authorization was granted.

Patients in the treatment cohort were treated based on the St. Jude AML 08, COG AAML0523 and COG AAML0531 protocols. Down syndrome patients were treated based on the COG AML0431 protocol. It was noted whether the patient was treated on study or not.

Cytogenetic-risk groups were identified based on cytogenetic data collected at the time of diagnosis. The cytogenetic profiles recorded included t(8;21), inversion 16, trisomy 11, monosomy 7, monosomy 5, trisomy 21, normal or unknown profiles.

Outcomes were recorded from diagnosis until recovery from the final course of treatment. However, any outcome or complications which occurred during induction were emphasized given that patients are most susceptible to becoming neutropenic and being at greatest risk for complications during that phase. Infectious complications that were specifically recorded included bacteremia, septic shock, pneumonia, urinary tract infection, cellulitis, *Clostridium difficile* colitis, fungal infections and other infectious complications the patient may have sustained during their treatment. Infectious complications that occurred during induction, total treatment course, and if the patient relapsed and had to undergo re-induction were analyzed separately. For each patient, any modifications to their standard antibiotic course, exact reasons for the modification and the antibiotics that were added or removed were examined during induction, entire treatment course and if applicable during induction and re-induction. For those patients who were bacteremic during any time during their treatment, microbiological records were analyzed for which organisms grew from their blood cultures and the organisms' antibiotic sensitivities.

Response to AML treatment after conclusion of therapy was categorized as refractory disease, continuous first remission, remission after relapse (second complete remission), alive after disease relapse, death from treatment or death from disease. Of those who relapsed, data on whether they achieved second remission were examined as well.

Other data variables collected comprised of any Pediatric Intensive Care Unit (PICU) stays during induction or throughout the entire treatment, history of a hematopoietic stem cell transplant (HSCT), whether the patient was on a special low bacteria diet while neutropenic (ANC <300). The basic guidelines of a neutropenic diet consisted of avoidance of all uncooked meat, fish, vegetables and fruit. Patients are also to consume only pasteurized dairy products and avoiding soft mold-ripened and blue-veined cheese.

In order to determine the effect of aggressive supportive measures on OS, EFS, and TRM, outcomes of the Treatment Cohort with be compared with outcomes of the control cohort. Historical data from of pediatric patients treated on COG AML protocols were utilized for comparison to the treatment cohort. Data from the CCG-2961 (treated August 1996 and December 2002) and COG AAML0531 (treated between August 2006 to June 2010) studies were used to compare the RCHSD OS, EFS and TRM to the results of these protocols.

Results

There were 35 AML patients that were included in the treatment cohort. Of these children, two individuals left RCHSD to complete their treatment at different institutions located in Orange County and Mexico. The third infant with suspected AML died several days after birth as a result of severe pulmonary hypertension and birth complications. These three children were not included in the final analysis. Four of the patients had a diagnosis of Down syndrome. Demographics of the patients are described in Table 1.

Table 1. Characteristics of the children with de novo AML treated at RCHSD between January 2006 and July 2013

Characteristic		
	Number	Percentage
Gender		
Female	19	54.3
Male	16	45.7
Age, y		
0-1	10	28.6
2-16	22	62.9
≥17	3	8.5
Ethnicity		
Non-Hispanic Caucasian	9	25.7
African-American	2	5.71
Hispanic	13	37.4
Asian	3	8.6
Mixed*	2	5.71
Other	6	17.1
Down Syndrome		
Yes	4	11.4
No	31	88.6
FAB Classification		
M0	0	0
M1	2	5.9
M2	3	8.8
M4	9	26.5
M5	4	11.8
M6	1	2.9
M7	5	14.7
AML NOS	10	29.4
Cytogenetics		
High-Risk	8	21.6
Intermediate Risk	15	40.5
Low Risk	8	21.6
Other	5	13.5
Unknown	1	2.7
Treatment Protocol		
AAML0431	3	9.1
AAML0523	1	3.0
AAML0531	21	63.6
AAML0532	1	3.0
St. Jude AML08	7	21.2
CNS Involvement		
Yes	10	29.4
No	22	64.7
Inevaluable	2	5.9
History of HSCT		

Yes	12	38.7
No	23	61.3

*Mixed ethnicity: identified as both non-Hispanic Caucasian and African-American. Another patient identified himself as both Hispanic and Asian.

Relapse risk group parameters are based on cytogenetic profile. Cytogenetic profiles were deemed low, intermediate or high risk per guidelines outlined in the AAML0531 protocol. High-risk was defined as monosomy 7, monosomy 5, 5q deletions or those with complex cytogenetics. Intermediate Risk was defined as either normal, trisomy 8, trisomy 21, 7q deletion, 9q deletion, abnormal 11q23 and any other structural or numerical changes. Low risk was defined as inversion 16/t(16;16) or t(8;21) cytogenetics. There were some patients that had multiple cytogenetic profiles.
For those whose cytogenetics were classified as "other", three patients had translocations of chromosomes 9 and 11, one individual had translocation of chromsomes19 and 11 and one patient had translocation of chromosomes 1 and 11. One individual's cytogenetic profile was unknown because insufficient marrow was extracted during his bone marrow aspirate and biopsy.

Figures 1, 2 and 3 depict Kaplan Meier curves showing the OS, EFS and TRM respectively of all patients treated at RCHSD. The number of survival days was calculated using the date of AML diagnosis as the start time. The time difference between this date and either the date of death or the present day, marked as February 18, 2014 at which time data was collected.

Figure 1: Overall Survival of Pediatric Patients treated at RCHSD from January 2006 to July 2013

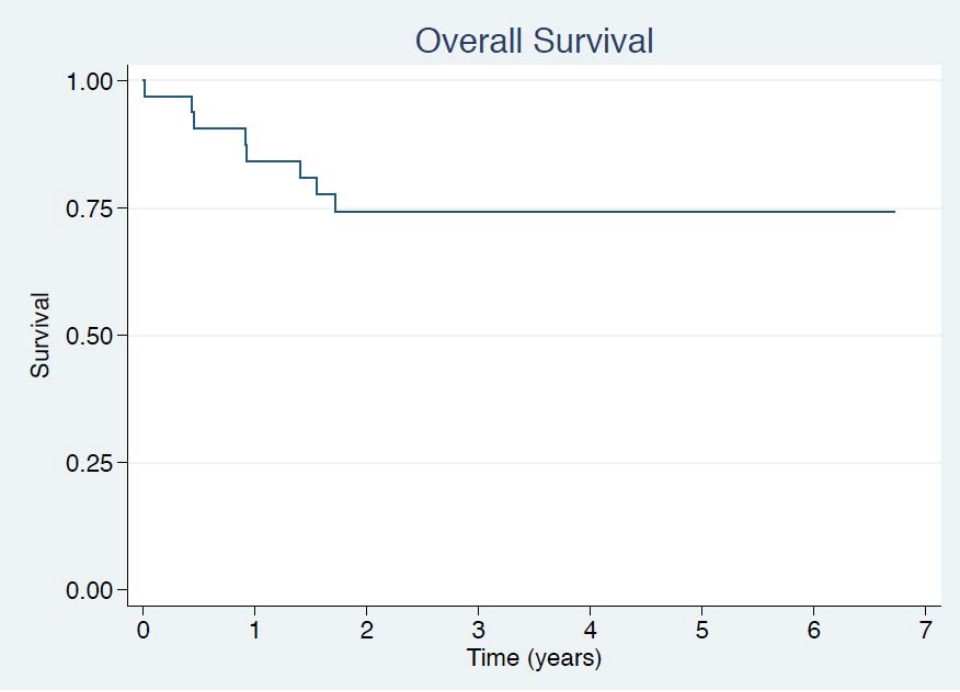


Figure 2. Event Free Survival of Pediatric Patients treated at RCHSD from January 2006 to July 2013

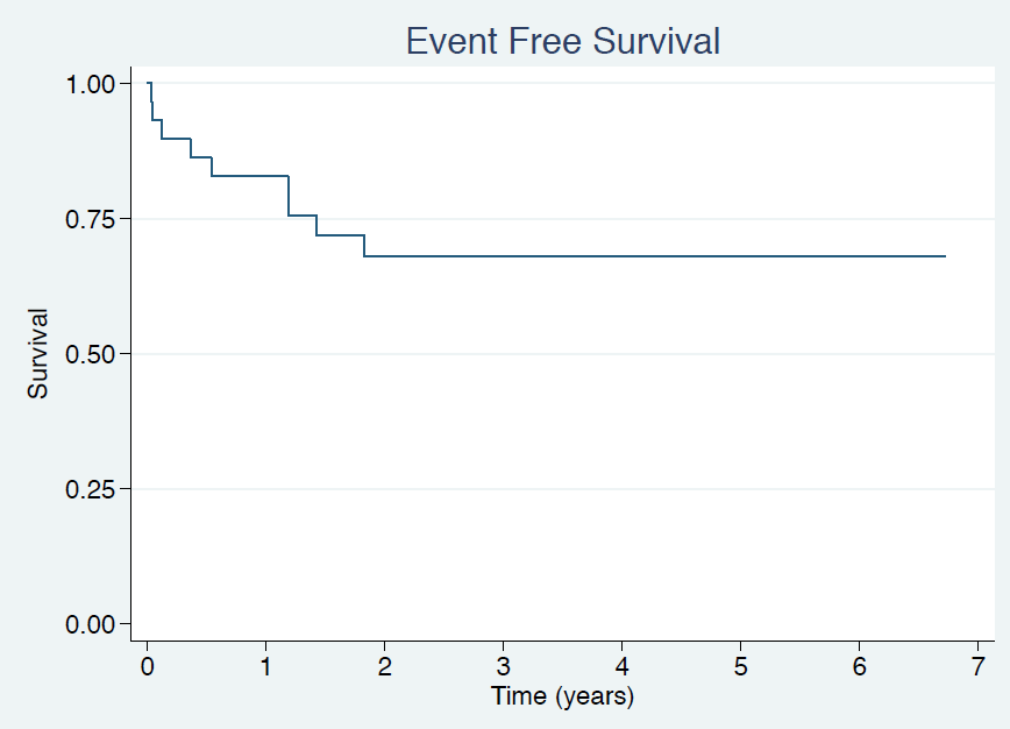
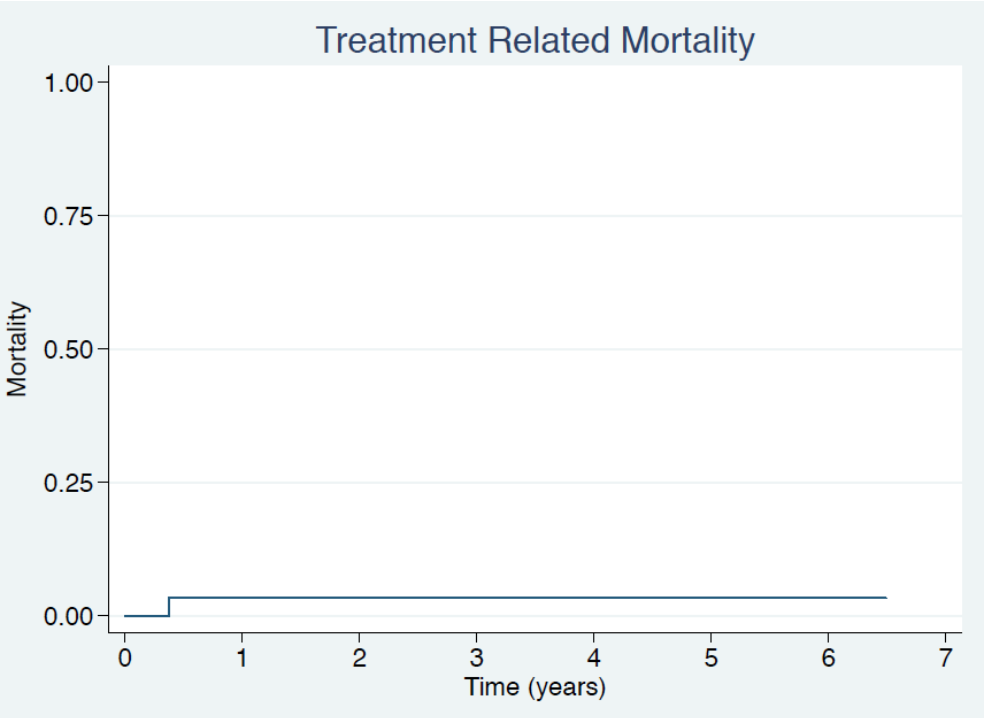


Figure 3. Treatment Related Mortality of Pediatric Patients treated at RCHSD from January 2006 to July 2013



From these results, OS for AML patients treated at RCHSD was 75%, EFS was 59% and TRM was calculated as 3%. These values were compared to the OS, EFS and TRM of patients treated on the COG AAML0531 and CCG2961 protocols. Only one individual died from treatment related causes making TRM 3%.

Table 2 compares the CR, TRM, EFS and OS of patients treated at RCHSD between January 2006 and July 2013 to those patients treated on protocols AAML0531 and CCG2961. Patients treated at RCHSD had a TRM of 3%

compared to those treated on AAML0531 and CCG2961. TRM for CCG2961 pre-amendment was 19% and 12% post-amendment. EFS for RCHSD patients was 59%, greater than the percentages of those patients treated on the other two protocols. OS was 75% which was also greater than the OS of both protocols.

Table 2. Comparison of CR, TRM, EFS and OS among RCHSD treated patients and AAML0531 and CCG2961 patients.

	RCHSD	AAML0531 Arm B	AAML0531 Arm A	CCG2961	
Treatment Related Mortality (TRM)	3%	9%	6%	19%	12%
Event Free Survival (EFS)	59%	53%	47%	46%	
Overall Survival (OS)	75%	69%	65%	57%	

A secondary aim of this study was to analyze the infectious complications patients had during induction and total duration of therapy. Table 2 summarizes the infectious complications patients had during induction or throughout treatment course. For those individuals who relapsed after achieving first remission, the cumulative infectious complications during re-induction and induction were noted as well. During the entire course of treatment, bacteremia was the most common infectious complication representing 46.7% of the total infectious complications recorded. Diarrhea due to Clostridium difficile (C. difficile) comprised 16.5% of the infectious complications throughout the full length of treatment. During induction, bacteremia comprised of 33.3% of the infectious complications with diarrhea due to C. difficile comprising 28.6% of the events. A similar trend is observed among the patients who relapsed and underwent re-induction with bacteremia and C. difficile colitis comprising 30.8% and 26.9% of the infectious complications respectively.

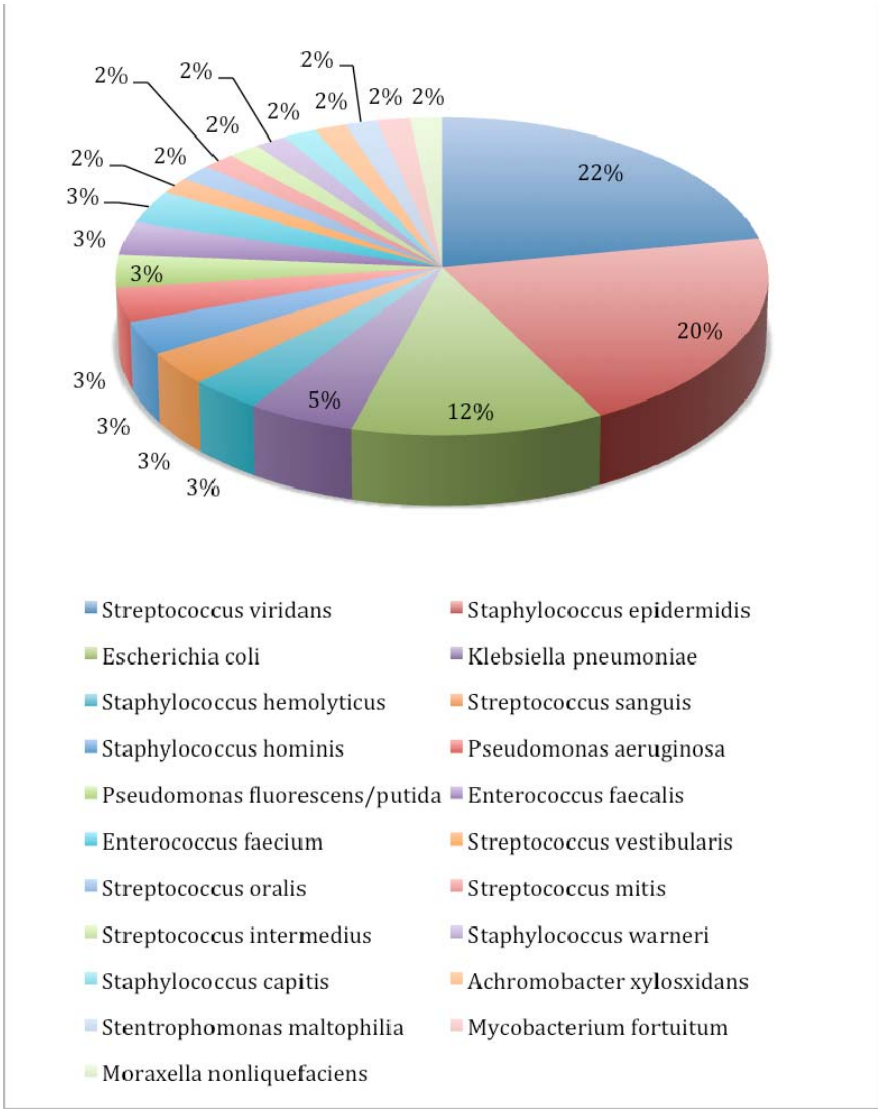
Table 3. Infectious Complications of AML Treatment Cohort during Induction, Re-Induction and Total Course of Therapy

	Induction		Induction and Re-Induction		Total Duration of Therapy	
Infectious Complication	Number	%	Number	%	Number	%
Bacteremia	7	33.3	8	30.8	43	44.3
Septic Shock	0	0	3	11.5	2	2.1
Pneumonia	0	0	1	3.9	8	8.2
Urinary Tract Infection	1	4.8	1	3.9	4	4.1
Cellulitis	4	19.0	3	11.5	7	7.2
C. difficile colitis	6	28.6	7	26.9	16	16.5
Fungal Infections	0	0	0	0	5	5.2
Other	3	14.3	3	11.5	12	12.4
Total	21	100	26	100	97	100

Given that bacteremia was the most common infectious complication among patients, we analyzed the specific organisms that grew from patients' blood cultures. Figure 1 depicts these results. Streptococcus viridans (22%) and staphylococcus epidermidis (20%) were the most common organisms that grew from patients' blood cultures. Gram-positive organisms comprised 69% of the isolates from blood cultures and Gram-negative

organisms made up 29% of isolates. There were several positive blood cultures that were attributed to contamination and not included in the analysis. One patient had a positive blood culture for Lactobacillus species that was thought to be a contaminant as the organism grew out seven days after the specimen was collected. The second patient had a positive blood culture that had been negative for four days and then on day 5 grew out Streptococcus parasanguis. The last patient had a positive blood culture that grew out Corynebacterium species after several days of negative cultures.

Figure 4. Organisms that grew from positive blood cultures



Given that patients had various antibiotic regimens as a result of different infectious complications, we looked into the various antibiotic modifications made to initial empiric therapy. Antibiotic modifications were examined for during induction, re-induction and at completion of therapy. Table 3 describes the reasons patients had to modify their standard antibiotic regimen along with which antibiotics were added to augment their therapy.

Table 3. Antibiotic Modifications made during total course of treatment

Reason for Modification	Number (#)	Description of Modification

1. Resistant organism identified		
Strep viridans	10	Added vancomycin
	2	Added cefepime
Methicillin sensitive staph aureus (MSSA)	1	Added vancomycin Added nafcillin
Strep vestibulans	1	Added vancomycin
Strep sanguis	1	Added vancomycin, imipenem penicillin G, and levoquin
Strep intermedius	1	Added meropenem
	1	Added linezolid
Strep oralis	1	Added vancomycin
Staph epidermidis	8	Added vancomycin
	2	Added gentamicin
	1	Added linezolid
	1	Added clindamycin
Staph hemolyticus	1	Added rifampin
Staph hominis	1	Added vancomycin
Enterococcus faecalis	2	Added gentamicin, ampicillin Added ceftaroline
Enterococcus faecium	1	Added vancomycin
Escheria coli	2	Added cefepime
	1	Added meropenem
	2	Added tobramycin
Pseudomonas fluorescens	1	Added tobramycin Added meropenem
Pseudomonas aeruginosa	1	Added tobramycin
Klebsiella Pneumoniae	1	Added tobramycin
Stenotrophomonas maltophilia	1	Added ceftazidime
Mycobacterium fortuitum	2	Added amikacin, levoquin and clarithromycin
	1	Added ciprofloxacin
Acrhomobacter xylosxidans	1	Added meropenem
Unspecified (Gram positive cocci in clusters)	1	Added vancomycin
2. Clinical Deterioration	2	Added vancomycin
	1	Added ambisome
3. Persistent Fever	29	Added vancomycin
	1	Added ceftriaxone
	1	Added ciprofloxacin
	2	Added linezolid
	4	Added Ambisome
	1	Added Abelcets
4. Allergic Reaction	2	Added other (pentamidinebecause of reaction to Bactrim)
	6	Added meropenem
	1	Added linezolid
	1	Added posoconazole
5. C. difficile colitis	18	Added metronidazole
6. Documented Fungal Infection	1	Added abelcet
	1	Added micafungin
7. Other (specify)		

Cellulitis	2	Added Ancef
	2	Added vancomycin
	1	Added nafcillin
Dental Infection	1	Added clindamycin (dental infection)
Presumed fungal pneumonia	2	Added micafungin
	2	Added ambisome
	1	Added abelcet
	1	Added vancomycin
Study protocol	1	Added ciprofloxacin
Drug reaction	1	Added linezolid (red man syndrome from vancomycin)
Pneumonia	1	Added ceftriaxone and azithromycin
History of positive MTB cultures	1	Added ethambutol, pyrazinamide
Otitis media	1	Added clindamycin
	1	Added vancomycin, ceftazidime, tobramycin and zosyn
		Added vancomycin
Healing ulcer	1	Added vancomcyin
Perineal lesions	1	Added vancomycin
Inguinal abscess	1	

Of the patients where a resistant organism was identified, Strep viridans and Staph epidermidis were the two most common organisms to grow from culture. Vancomycin was the most common antibiotic modification made when either of these organisms were identified. A similar trend was seen for those patients where antibiotics were modified due to persistent fever. Diarrhea due to C. difficile infection was a common infectious complication seen among patients during treatment in which all patients were treated with a course of metronidazole. Two fungal infections were distinctly identified through microbiological studies requiring addition of micafungin and abelcet. Other reasons necessitating antibiotic modifications were numerous and a wide variety of antibiotics were used to treat the specific medical requirements of each patient.

During the collection of data, it was found there were patients who required admissions to the pediatric intensive care unit (PICU) for higher level of care. Data on PICU admissions during induction and total course of therapy were documented if the patient was admitted for infectious complications and respiratory distress which may or may not have required ventilatory support. Those patients who were admitted to the PICU with leukocytosis and required leukophoresis were excluded.

Table 4. Number of admitted PICU days during Induction and throughout entire treatment for septic shock and ARDS.

	Induction		Total Treatment Course	
	N	%	N	%
Number of patients requiring PICU admissions	4	12.5	6	18.8

There were numerous reasons certain children were admitted to the PICU during their treatment course. One child was admitted for observation for prolonged fever and low ANC. Another child required aggressive fluid resuscitation for blood pressure control. Three children were admitted for leukophoresis due to leukocytosis. Four children required PICU stays for stabilization after beginning to exhibit signs of septic shock. Three individuals required oxygen support by mechanical ventilation due to respiratory distress, but four children were admitted for respiratory distress but did not require mechanical ventilation. One child was intubated post-operatively after bronchoscopy and sent to PICU for observation of respiratory status.

Discussion

By reviewing the records of de novo AML patients treated between January 2006 and July 2013 after oncologists at RCHSD implemented an intensive supportive care protocol for pediatric patients we made several important observations. First, the OS, EFS and TRM of the patients analyzed who were treated at RCHSD were 75%, 59% and 3% respectively. Additionally, when comparing patients treated at RCHSD and AAML0531 and CCG2961 studies, OS and EFS were both greater than the measured OS and EFS of either of these protocols. TRM was also less than patients treated on AAML0531 and CCG2961. The differences in OS, EFS and TRM of the different protocols used to treat patients at RCHSD could not be analyzed given the small population size and did not have enough power to observe any differences.

Based on these findings, there was a benefit for the AML patients treated on the intensive supportive care protocol that required patients to remain hospitalized until neutrophil nadir and recovery. There was an advantage in utilizing measures such as instituting empiric antibiotic and antifungal therapy, initiating low bacteria diets for AML patients with ANC <300 as demonstrated in the OS, EFS and TRM. This is in direct contrast to the COG review that did not demonstrate a statistically significant benefit in keeping patients in the hospital during profound neutropenia.

In analyzing the data for secondary aims, there were also some other important observations made. Bacteremia and C. difficile colitis were the most common infectious complications patients had among the treatment cohort both during induction and throughout course of therapy. In effect, *S. viridans and S. epidermidis* were the two most common organisms that grew from blood cultures of bacteremic patients. The overall incidence of infectious complications is comparable to the two studies previously mentioned. The multi-center Italian study that showed bacteremia was seen in 32% of patients throughout their entire treatment course while bacteremia was an infectious complication seen in 44% of patients treated at RCHSD. Gram-positive bacteria comprised a majority of the bloodstream isolates of RCHSD AML patients, similar to the findings reported by Lehrnbecher *et al.* Among the antibiotic modifications made throughout the patients' treatment courses, the addition of vancomycin was the most common change made. Given that a majority of the isolates from blood cultures were Gram-positive species, there should be consideration in the future of potentially adding vancomycin as part of empiric therapy.

Additionally, the results of the COG review stated that mandatory hospitalization was associated with an increased rate of C. difficile infections, which is consistent with the observations of this report. Of the patients treated at RCHSD who contracted C. difficile associated diarrhea, this most commonly occurred during

induction (28.6%). Of all the patients who had C. difficile infection throughout the entire course of treatment, it comprised 16.5% of all total infectious complications. Lehrnbecher *et al* identified the causative organism of diarrhea as C. difficile in the stool of 26 of the 43 patients with diarrhea. Other organisms identified included rotavirus (14), Salmonella spp (2) and adenovirus (1). Based on these results, if an organism cannot be identified empirically treating a patient with diarrhea of unknown cause with a course of metronidazole may be beneficial given this is the most common cause of infectious diarrhea.

While the study population analyzed in this study is small in comparison to other trials, this report has several advantages. While there have been previous studies done that have provided information and insight into the epidemiological relevance of OS, EFS, TRM and infectious complications among AML pediatric patients, this study aims to add more detailed information to this growing pool of knowledge. It also adds a way to evaluate the epidemiology of infectious complications and survival outcomes among AML patients who received therapy through RCHSD, potentially providing insight into the efficacy of current practices. However, one disadvantage is that this study is small in size and does not have enough power to observe any statistical differences in the OS, EFS and TRM among those RCHSD patients treated with different protocols. Additionally, this study is retrospective in nature and does not have a true control group to make direct comparisons to.

In conclusion, the intensive supportive care protocol for pediatric AML patients treated at RCHSD had a positive effect on OS, EFS and TRM. This is supported by the direct comparisons made to those children treated on the CCG-2961 and AAML0531 protocols. Also, infectious complications are very common among AML patients during treatment with bacteremia and C. difficile colitis being the most frequently identified throughout course of treatment. Gram-positive organisms were the most commonly bloodstream isolates among bacteremic patients with the addition of vancomycin as the most common antibiotic modification made. Further considerations should include the addition of vancomycin as a prophylactic antibacterial agent and metronidazole as empiric therapy for those with diarrhea, even with unknown causes. The information from this study could potentially be used to design a future prospective study to analyze the outcomes of pediatric patients treated under the same parameters as this cohort. Based on these findings, mandatory hospitalization of patients until count recovery prior to hospital discharge and the use of empiric antibacterial and antifungal therapy to manage febrile neutropenia improves outcomes for these patients.

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