Original Article

Evaluating the consequences of critically ill patients with pediatric cancer at Aliasghar Children's Hospital

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Abstract

Background: Despite significant progress in supportive care and advancements in chemotherapy treatments, cancer remains a leading cause of mortality in children. The objective of this study was to assess the potential correlation between various risk factors and the consequences of patients with pediatric cancer who were admitted to the pediatric intensive care unit (PICU). **Methods:** The present investigation is a retrospective cohort study that examined children with cancer who were between the ages of 1 month and 17 years and had been admitted to the PICU. Demographic and clinical information of all patients, including such as the age, type of cancer, sex, BMI, history of specific disease, PICU admission time, disease condition on PICU admission, patient's status at PICU admission, and number of organ failures, were extracted from each patient file. **Results:** The number of pediatric oncology patients admitted to the PICU was 127. The highest mortality rate was observed among children with heart problems (75%), followed by CNS involvement (54.2%) and sepsis (42.9%). The study found that various factors had a significant effect on the outcomes of patients who were admitted to the PICU, including but not limited to the primary type of malignancy, disease status, indications for hospital admission, patient's condition, inpatients' length of stay (LOS), tumor type, and the extent of organ failure at the time of admission to the PICU. **Conclusion:** Despite recent advancements in healthcare, the prognosis of patients admitted to the PICU in underdeveloped areas remains suboptimal in comparison to those in developed regions. Poor outcomes were found to be significantly associated with various factors, including the primary type of malignancy, disease status, the reason for admission to the PICU, patient's condition, LOS, tumor type, and the extent of organ failure, especially in cases involving hematological malignancies.

Keywords: Consequences of disease, mortality, patients with pediatric cancers, PICU

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Introduction

Over the past few decades, significant progress has been made in diagnosing pediatric cancer, leading to a noticeable rise in the 5-year survival rates of pediatric cancer patients, from 40% in 1970 to 80% in 2000.[1] This improvement in survival rates is likely due to the use of advanced therapies for cancer, as well as advances in supportive care for cancer patients. However,

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the use of treatments for progressive cancers is associated with some complications in children, such as life-threatening situations and eventually hospitalization in the pediatric intensive care unit (PICU).[2] Studies have shown that approximately 33% of children diagnosed with cancer require admission to the PICU at least once during their treatment.[3,4] Typically, children diagnosed with cancer are admitted to the PICU due to a range of tumor-related concerns, such as tumor lysis syndrome, as well as treatment-related issues such as immunosuppression and infection.[3] Several investigations have indicated unfavorable consequences in cancer patients admitted to the PICU, particularly in those who need mechanical ventilation or other forms of internal assistance for sepsis following bone marrow transplantation.[5] Recent studies conducted in developed countries have demonstrated encouraging results, In high-income countries, the 5-year survival rate for childhood cancer is over 80%. However, in low- and middle-income countries, the 5-year survival rate is less than 40%. (we wrote it based on cited articles in the manuscript. We just changed percentage to ratio (proportion)).[6,7] These studies have endeavored to identify diagnostic factors that are significantly associated with disease outcomes at the time of admission to the PICU. This information can aid physicians in determining the most appropriate and effective treatment strategies for their patients. Studies have identified several disease- and patient-related factors that may lead to unfavorable outcomes in cancer patients who are admitted to the PICU. These factors include but are not limited to age, type of cancer, the stage of disease, recovery status, and response to chemotherapy.[8] However, some of these factors have not been reported as negative diagnostic consequences in other studies.[9,10] Despite recent advancements in healthcare, there is still a lack of comprehensive information on disease outcomes in pediatric cancer patients admitted to the PICU, particularly in developing countries. As such, there is a need for more in-depth studies with larger sample sizes to better understand the factors that contribute to these outcomes. The identification of such factors is critical in both the diagnosis of disease outcomes and the effective management of these conditions. Therefore, the primary objective of this study was to investigate and analyze the consequences and the risk factors related to pediatric cancer patients admitted to the PICU.

Methods

For this retrospective cohort analysis, all children diagnosed with cancer between the ages of 1 month to 17 years old who were admitted to the PICU at Ali Asghar Children's Hospital in Tehran, Iran, between 2013 to 2021 were included. The Ethics Committee of the Iran University of Medical Sciences approved the overall present research. Each patient's family provided written consent after being informed of the details of the study at the time of their admission. The data about patients was obtained from their files available at the time of their admission to the PICU. At the commencement of the study, a checklist was prepared, which contained details on the demographic and basic clinical information of all patients. These details included but were not limited to age, type of cancer, sex, BMI, medical history of specific diseases, time of admission to the PICU, condition of the disease at the time of PICU admission, patient's status upon PICU admission, and the extent of organ failure. According to the research protocol, patients with a medical history of congenital heart disease, diabetes, chronic respiratory diseases, and other genetic and congenital disorders were excluded from the cohort. Following this, patients were allocated into three separate groups based on their disease outcomes: completed treatment, partial recovery, and expired patients. Eventually, the relationship between patient outcomes and these basic demographic and clinical characteristics was evaluated.

Statistical analysis

The study employed various statistical methods to analyze quantitative data. Descriptive statistics were used to summarize the data, and the mean value along with standard deviation (SD) (Mean ± SD) was presented. To compare the percentage or frequency of different parameters across groups, crosstabs and Chi-square tests were employed. In addition, the one-way ANOVA test was utilized to compare the mean value of parametric data across three groups. A significance level of $P < 0.05$ was deemed statistically significant. The data were analyzed using the statistical software SPSS (IBM, version 19).

Results

The study included a sample of 127 cases with a mean age of 55.65 ± 44.51 months. Table 1 provides a summary of the basic demographic and clinical characteristics of all the cases examined. In total, 91 patients (52.9%) were boys and 81 cases (47.1%) were girls. Twenty-eight out of 172 patients (16.27%) were new cases who immediately underwent surgery (11 boys and 17 girls). In children, the most prevalent types of cancer were acute lymphocytic leukemia (ALL), accounting for 34.3% of cases, and Wilm's tumor, which accounted for 16.27% of cases. The mean BMI at the time of diagnosis and admission was 16.90 ± 2.64 kg/m^2 and 16.96 ± 2.60 kg/m^2, respectively. Forty-seven (32.6%) patients showed complete treatment, 38 (26.4%) had partial treatment, and 59 patients (40.97%) died. Of the 28 new cases that were operated on, 24 patients (85.7%) were completely cured, two patients (7.1%) died, and two patients (7.1%) were partially cured. Sepsis was the most important reason for admission to PICU (34.3%). Regarding patient's condition at PICU admission, most of them had MOF (30%) and oxygen therapy (25%). Approximately 19.4% of children had stable status during admission to PICU. More than half of the patients (65.7%) had hematologic tumor type.

Table 2 displays the association between the consequences of the disease and basic demographic and clinical characteristics across all cases examined. No significant association was found between disease consequences and age, sex, or BMI. A statistically significant association was observed between the consequences of disease cancer types ($P < 0.001$). Children with HLH had the highest mortality rate (89.5%), followed by those

Table 1: Basic demographic and clinical characteristics of patients

Variables	Results
Age (Month)	55.65±44.51
Gender	
Boys (%)	91 (52.9%)
Girls (%)	81 (47.1%)
BMI at admission (kg/m^2)	16.95±2.74
BMI at diagnosis (kg/m^2)	17.0±2.71
BMI range at admission	
Underweight	78 (54.2%)
Healthy weight	61 (42.4%)
Overweight	2 (1.4%)
Obese	3 (2.1%)
Type of cancer	
ALL (%)	34.3%
Wilm's (%)	16.27%
AML (%)	8.72%
NHL (%)	9.88%
HD (%)	1.16%
Neuroblastoma (%)	8.72%
CNS tumors (%)	4.06%
GCT (%)	1.74%
HLH (%)	11.04%
Adrenal tumor (%)	2.90%
Rhabdomyosarcoma (%)	1.16%
PICU admission time	7.13±5.92
Disease condition on PICU admission	
CR	71 (49.3%)
Relapse	73 (50.7%)
PICU cause admission	
Sepsis	38.9%
Post-surgery	5.6%
CNS condition	16.7%
TLS	2.1%
Respiratory distress	12.5%
GIB	3.5%
Electrolyte imbalance	4.2%
Renal failure	1.4%
Heart failure	8.3%
Pneumonia	6.9%
Patient status at PICU admission	
Stable	19.4%
Unstable	0.7%
MOF	29.9%
Ventilator	23.6%
O_2 therapy	24.3%
Dialysis	0.7%
Post-CPR	0.7%
Tumor type	
Hematologic (%)	65.70%
Solid (%)	34.30%
Number of organ failures	0.98±1.22

with CNS tumors (71.4%). A statistically significant association was found between disease status at the time of admission to the PICU and disease outcomes ($P < 0.001$). Furthermore, 89.4% of the recovered patients were in the CR group, but 81.4% of the deceased patients were in the relapse group. The highest mortality rate was observed among children with heart problems (75%), followed by CNS involvement (54.2%) and sepsis (42.9%). The highest complete recovery was observed among patients with electrolyte disorders (83.3%). There was also a significant relationship between the patient's condition during hospitalization in PICU and disease outcomes ($P < 0.001$). Patients who had stable conditions exhibited the highest frequency of complete recovery (82.1%), while those receiving complete oxygen therapy had a frequency of 62.9%. The highest frequency of mortality was observed among patients with post-CPR and MOF (100% and 97.7%, respectively). A statistically significant association was observed between the consequences of disease and the duration of hospitalization in the PICU ($P = 0.011$). The mean hospitalization time in patients with complete treatment (5.02 days) was significantly shorter than that in patients with partial recovery (8.13 days) and those who expired (8.17 days). A statistically significant correlation was found between the consequences of disease outcomes and tumor type ($P = 0.02$). While approximately 44.6% of patients with hematologic tumors died, about half of patients with solid tumors completely recovered. A statistically significant association was observed between the consequences of disease and the degree of organ failure ($P < 0.001$). The average number of organ failures in patients with complete (0.04) and partial recovery (zero) was significantly lower than that in deceased patients (2.36).

Discussion

This study aimed to investigate the correlation between various basic demographic and clinical characteristics and disease outcomes in pediatric cancer patients who were hospitalized in the PICU. Among children admitted to the PICU, ALL was the most frequently diagnosed type of cancer. The mortality rate for children with cancer was 32.6%, whereas 26.4% of patients achieved complete recovery, and 35.5% exhibited partial recovery. We did not find a significant relationship between disease outcome with patients' age, sex, and BMI. Our findings showed that disease outcomes were significantly correlated to primary cancer type. The mortality rate in children with HLH was 89.5%, while it was 71.4% and 53.3% in children with CNS and AML, respectively. On the contrary, 100% of children with GCT were completely cured. Thus, this suggests that the underlying cancer type is a crucial determinant for forecasting the consequences of disease among the children who are hospitalized in the PICU. Our findings revealed a significantly higher mortality rate in patients who experienced a relapse of the disease compared to those who achieved complete recovery (81.4% vs. 18.6%). Notably, previous reports have cited mortality rates ranging from 50% to 60% for patients with relapsed disease. This variation may be attributed to the possibility that in our study, pediatric cancer patients admitted to the PICU were more likely to experience delayed diagnoses or hospitalization at an advanced stage of the disease. Thus, our findings suggest that disease relapse can be regarded as a significant risk factor for mortality in children with

Table 2: Relationship between disease outcome with basic demographic and clinical findings in all cases

	Complete treatment	Partial treatment	Expired	*P*
Age (month)	55.21±39.72	69.18±49.42	57.55±49.38	0.34
Gender				
Boys	26 (32.5%)	18 (22.5%)	36 (45%)	0.41
Girls	21 (32.8%)	23 (35.9%)	20 (31.3%)	
BMI at admission (kg/m^2)	16.79±2.34	17.58±3.19	16.68±2.71	0.25
BMI at diagnosis (kg/m^2)	16.70±2.18	17.84±3.25	16.69±2.61	0.08
BMI range at admission				
Underweight	27 (34.6%)	18 (23.1%)	33 (42.3%)	0.56
Healthy weight	19 (31.1%)	17 (27.9%)	25 (41.0%)	
Overweight	1 (50%)	1 (50%)	0	
Obese	0	2 (66.7%)	1 (33.3%)	
Type of cancer				
ALL (%)	17 (28.8%)	20 (33.9%)	22 (37.3%)	<0.001
AML (%)	3 (20%)	4 (26.7%)	8 (53.3%)	
NHL (%)	9 (52.9%)	5 (29.4%)	3 (17.6%)	
HD (%)	0	1 (50%)	1 (50%)	
Neuroblastoma (%)	11 (73.3%)	1 (6.7%)	1 (6.7%)	
CNS tumors (%)	0	2 (28.6%)	2 (28.6%)	
GCT (%)	3 (100%)	0	0	
HLH (%)	0	2 (10.5%)	2 (10.5%)	
Adrenal tumor (%)	3 (60%)	2 (40%)	2 (40%)	
Rhabdomyosarcoma (%)	1 (50%)	1 (50%)	1 (50%)	
PICU admission time	5.02±5.98	8.13±5.56	8.17±5.75	0.011
Disease condition on PICU admission				
CR	42 (89.4%)	18 (47.4%)	11 (18.6%)	<0.001
Relapse	5 (10.6%)	20 (52.6%)	48 (81.4%)	
PICU cause admission				
Sepsis	23 (41.1%)	9 (16.1%)	24 (42.9%)	<0.001
CNS condition	0	11 (45.8%)	13 (54.2%)	
TLS	1 (33.3%)	1 (33.3%)	1 (33.3%)	
Respiratory distress	5 (27.8%)	6 (33.3%)	7 (38.9%)	
GIB	1 (20%)	3 (60%)	1 (20%)	
Electrolyte imbalance	5 (83.3%)	1 (16.7%)	0	
Renal failure	0	2 (100%)	0	
Heart failure	0	3 (25%)	9 (75%)	
Pneumonia	5 (50%)	2 (20%)	3 (30%)	
Patient condition at PICU admission				
Stable	23 (82.1%)	4 (14.3%)	1 (3.6%)	<0.001
Unstable	0	2 (100%)	0	
MOF	0	1 (2.3%)	42 (97.7%)	
Ventilator	2 (5.9%)	17 (50%)	15 (44.1%)	
O_2 therapy	22 (62.9%)	13 (37.1%)	0	
Dialysis	0	1 (100%)	0	
Post-CPR	0	0	1 (100%)	
Tumor type				
Hematologic	30 (26.8%)	32 (28.6%)	50 (44.6%)	0.02
Solid	17 (53.1%)	6 (18.8%)	9 (28.1%)	
Number of organ failures	0.04±0.29	0	2.36±0.58	<0.001

cancer. In our study, a significant relationship was found between factors leading to admission to PICU and disease outcomes. Heart failure (75%) and CNS involvement (54.2%) were the most common risk factors for mortality among children, while 83.3% of children with electrolyte imbalance exhibited complete recovery. On the contrary, sepsis was the most common cause of hospitalization and mortality (66.7%) in new cases that underwent surgery. These data indicate that conditions leading to PICU admission are important risk factors in determining disease outcomes. Thus, these factors can be considered as predictors of mortality in children with cancer. The patient's status during admission to PICU was another significant factor associated with the disease outcomes. Our results revealed that approximately 82.1% of patients with stable conditions at the

time of admission to PICU showed complete treatment, while 97.7% of patients with MOF died. This finding emphasizes that a patient's condition is a very important risk factor affecting the disease outcomes and thus must be carefully evaluated during admission to the PICU to prevent mortality. Furthermore, we noted a negative correlation between disease outcomes and the duration of hospitalization in the PICU. Patients with complete recovery had a shorter hospital stay in PICU compared to expired patients. There was a significant relationship between tumor type and disease outcomes. While more than half of patients with solide-type tumors fully recovered, approximately 45% of patients with hematologic-type tumors died. Therefore, this indicates that the mortality rate in children with hematologic type tumors is much higher than in children with solid type tumors (44.6% vs. 28.1%), which needs further investigation. Similarly, our investigation revealed a statistically significant positive association between the consequences of disease and the extent of organ failure. With an increase in the number of organs failure, the mortality rate in patients significantly increased. Therefore, this issue can be considered as another important risk factor in the occurrence of mortality or disease outcomes.

In summary, our investigation revealed that multiple factors can influence disease outcomes in pediatric cancer patients who are admitted to the PICU. As a result, recognizing these factors is of utmost importance for effectively managing and preventing mortality in children. In general, primary malignancy, disease status at the time of PICU admission (recurrence or complete treatment), indication for PICU hospitalization, patient status during PICU hospitalization, duration of PICU hospitalization, tumor type, and the number of organ failure are important risk factors influencing the patients' outcomes. In this regard, several studies have evaluated the relationship between various risk factors and disease outcomes in children with cancer.

For instance, in a study conducted by Ali *et al.*,[11] a total of 550 children with cancer who were admitted to the PICU were examined. As reported by the authors, in 73.6% of the patients, hematologic malignancies were observed. The mean duration of hospitalization in the PICU was 5 days. As per the findings of the study, sepsis and respiratory disorders were identified as the principal reasons for hospitalization in the PICU. According to the findings, the survival rate of patients at the time of discharge from the PICU was 60%. The study also identified various factors that significantly influenced patient outcomes, such as the type of disease, reason for hospitalization, interventions administered, as well as the extent of organ involvement or injury upon admission to the PICU. These outcomes are consistent with the results of our investigation; we also observed hematologic malignancies as the most prevalent cancer type in children admitted to the PICU. Correspondingly, we identified a significant correlation between the average PICU length of stay and the consequences of the disease. Moreover, sepsis was the most important and common indication for hospitalization of children in the PICU. The highest mortality rate was observed among children with heart failure, followed by CNS involvement and sepsis. On the contrary, the most complete recovery was observed among patients with electrolyte imbalance. In a similar study, Dursun *et al.*[12] investigated the consequences of disease in 44 children with cancer who were hospitalized in the PICU. The duration of hospitalization in the PICU was 2–9 days, which was almost in line with our research findings. The most common type of malignancy was hematologic (81.2%). The mortality rate in all patients was 77.1%, which was almost twice the mortality rate reported in our study. Patients in the remission group exhibited a mortality rate of 11%, while those in the progressive disease and induction period groups had mortality rates of 93% and 88%, respectively. The most important indications leading to hospitalization in the PICU were respiratory disorders (60.4%), sepsis (25%), circulatory collapses (4.2%), and other factors (10.4%). Furthermore, they documented that inotropic agents, MOF, and mechanical ventilation were significantly linked with increased mortality rates in this patient population. In a recent meta-analysis study, Wösten-van Asperen *et al.*[13] reviewed 31 studies containing 1218 children with cancer admitted to the PICU. The overall mortality rate in these patients was 27.8%, which is close to what we found in our study (35.5%). In addition, the utilization of inotropic agents, mechanical ventilation, and continuous treatment for kidney transplantation were identified as factors that significantly impacted the consequences of disease and mortality rates in children with cancer admitted to the PICU. Sivan *et al.*[14] conducted a study involving 72 children with cancer who were hospitalized in the PICU. They demonstrated that the mortality rate in these children was approximately 51%. Mortality rates in children with acute disorders in multiple organs were significantly higher at around 66%. On the contrary, acute respiratory disorder was reported as the most common type of disorder (73%) and an important indication leading to hospitalization in PICU. Dalton *et al.*[15] evaluated the consequences of disease in 802 children with cancer who were hospitalized in 20 distinct PICU centers. The authors reported an elevated overall mortality rate in these patients, which was associated with factors such as the utilization of mechanical ventilation and administration of vasoactive agents. Some studies have also shown that systemic infections and lung disorders are some of the most important factors that lead to poor outcomes in these patients.[12,16,17] El-Nawawy *et al.*[18] demonstrated that the mortality rate of children with cancer who were hospitalized in the PICU was 38%. The authors also observed a significant association between multi-organ involvement and an elevated mortality rate in these patients. In addition, the percentage of sepsis and neurological disorders was significantly higher in deceased patients compared to those who achieved complete recovery.

Conclusion

To summarize, our study's results revealed that the following factors significantly affect the consequences of disease and increased mortality rates in pediatric cancer patients: the primary malignancy type, disease status upon admission to the PICU, reason for PICU admission, patient status, duration of hospitalization, tumor type, and the extent of organ failure.

Therefore, identification and evaluation of these risk factors to prevent mortality rates among children with cancer is recommended.

Ethics approval and consent to participate

The study protocol was approved by the ethics research committee, Iran University of Medical Sciences (IR.IUMS.FMD.REC.1398.085). All methods were carried out in accordance with Iran national committee for ethics in biomedical research relevant regulations and guidelines.

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Conflicts of interest

There are no conflicts of interest.

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