

Analysis of Causes and Risk Factors for Deaths Among Pediatric Oncology Patients: A 20-Year Observation

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Background: Despite major therapeutic advances, mortality among children with cancer remains a significant clinical problem, particularly treatment-related mortality (TRM). The aim of this study was to analyze causes of death and identify mortality risk factors in pediatric oncology patients.

Material and Methods: A retrospective single-center study was conducted in patients hospitalized for oncological diseases between 2004 and 2024. Seventy deceased patients were identified. A matched control group of survivors ($n=70$), adjusted for sex, age, and diagnosis, was included. Demographic, clinical, and laboratory data were analyzed using univariate and multivariate logistic regression.

Results: During the study period, 70 children died in hospital. Most were boys (61.4%), with a median age of 130 months. Hematological malignancies accounted for 64.3% of diagnoses. The leading cause of death was disease progression (69.6%), followed by TRM (31.4%), including infection-related mortality (IRM). Independent predictors of death were older age (OR=1.083, 95% CI: 1.006–1.166) and lower platelet count at diagnosis (OR=0.623, 95% CI: 0.456–0.851). Post-hematopoietic stem cell transplantation (HSCT) status was an independent predictor of infectious death (OR=4.04, 95% CI: 1.04–15.61).

Conclusion: Mortality in pediatric oncology remains clinically relevant, with a substantial proportion attributable to potentially preventable treatment-related causes. Early risk stratification and intensified supportive care are particularly important in older patients, those with thrombocytopenia, and post-HSCT patients.

Keywords: mortality, cancer, child, risk factors, leukemia, lymphoma

Introduction

Every year, approximately 300,000 children worldwide are diagnosed with cancer.¹ Thanks to significant advances in medical technology and the development of new lines of treatment, the cure rate for these diseases is now as high as 85%.² These results vary significantly between high-income countries (HICs) and low- and middle-income countries (LMICs) (survival rate of approximately 30%).¹ Unfortunately, regardless of the region of the world, cancer is one of the leading causes of child mortality, accounting for a total of 7% of deaths in the 5–19 age group.³ In HICs, they are second only to accidents and injuries, and in LMICs, they are second only to infectious diseases.^{3,4} Although cancer mortality in the pediatric population has decreased by 24–33% over the past 20 years, it remains a significant problem.^{5,6} In the US and UK, deaths were mainly caused by the progression of the underlying disease and were most common in brain tumors.^{5,6} In LMICs, the main cause of death in pediatric cancer patients was treatment-related mortality (TRM) – 14–66%, including infections (60%).^{7,8} Key contributors to treatment-related mortality (TRM) include severe infections, particularly bacterial or fungal sepsis during prolonged chemotherapy- or transplant-related neutropenia, when impaired innate immunity and mucosal barrier injury markedly increase the risk of rapid organ dysfunction and death. Additional major causes are direct treatment toxicities (eg, cardiopulmonary failure, hepatic veno-occlusive disease, renal injury, mucositis with nutritional compromise) and HSCT-specific complications such as acute/chronic graft-versus-host disease, graft failure, endothelial syndromes, and opportunistic infections related to prolonged immunosuppression.^{9–11}

Understanding the epidemiology and causes of child deaths is crucial because it allows for the implementation of appropriate modifications to therapy or prevention, especially in the case of TRM. Despite the availability of epidemiological data from large registries, information on the direct causes of death in children with cancer at the level of individual centers remains limited. Local analyses may reveal specific risk factors related to the organization of care, the availability of supportive therapies, and the profile of treated cancers that are not apparent in population-based studies. Data from Central and Eastern Europe on the direct causes of death in pediatric oncology remain limited, which makes regional analyses particularly valuable, especially in a study with such a long follow-up period as the one presented here.

The aim of this study was to analyze the causes of death in patients with cancer at a single academic center in eastern Poland.

Materials and Methods

A retrospective analysis of medical records of oncology patients hospitalized and deceased at the University Children's Hospital between January 2004 and December 2024 was conducted. Demographic (age, gender) and clinical data (diagnosis, clinical symptoms, laboratory test results, past infections, treatment used, cause of death) were recorded. The inclusion criteria for the study were: previously confirmed oncological diagnosis, age < 18 years (met by all patients due to the nature of the facility), full availability of medical records, including death certificates. The exclusion criteria were: no confirmed oncological disease or death before confirmation of the diagnosis, incomplete medical records, death outside the hospital (if the records did not contain relevant data on the circumstances). In order to perform an appropriate statistical analysis, a control group ($n=70$) was also included in the study. The control group consisted of patients in remission who had completed treatment, with identical diagnoses to those in the study group, and was also matched for gender and age. The data was stored on electronic devices at the hospital in an anonymized form, in compliance with all personal data protection rules. Parents or legal guardians of patients younger than 16 years provided written informed consent for the use of medical data for scientific purposes. Patients aged 16 years and older additionally provided assent/consent according to institutional regulations. All activities were carried out in accordance with the principles of the Helsinki Declaration. Approval was obtained from the Bioethics Committee at Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland (number KB 263/22). The above approval was granted for all pediatric oncology and hematology centers in Poland, on research into causes of death and infections among children with cancer. This study presents the results of research conducted at the center in Lublin, which is part of a nationwide study coordinated by the center in Bydgoszcz.

Statistical Analysis

For statistical analysis, MedCalc 15.8 software (MedCalc Software, Ostend, Belgium) was used. Before performing the actual statistical calculations, a power analysis was performed. The power of the test was 0.8. Based on this, the size of the study group was determined to be sufficient to consider the results significant. A value of $p < 0.05$ was taken as the criterion for statistical significance. Descriptive statistics were presented by the median and interquartile range (IQR), and nominal categorical variables were presented by the frequency and percentage (%). The D'Agostino–Pearson test was used to analyze normal distribution. Continuous variables were compared using Student's *t*-test (variables with a normal distribution) or the Mann–Whitney *U*-test (variables with a distribution different from normal). Categorical variables were compared using Pearson's chi-square test. Factors associated with death were analyzed using logistic regression, presenting the results as odds ratios (OR) with 95% confidence intervals (95% CI). Multivariate models included variables that were significant in univariate analyses or considered clinically relevant. Analyses of factors associated with the type of death (infectious death and death related to treatment complications) were performed only in the group of deceased patients. Scaling for age readability was set at 1 year (12 months) and for platelet count at 100 G/L.

Results

Study Group Characteristics

During the years analyzed, 70 oncology patients died in the hospital. Among these individuals, the vast majority were patients diagnosed with hematopoietic or lymphatic proliferative diseases or myelodysplastic syndrome (MDS) ($n=46$,

64.3%), followed by those with central nervous system tumors (n=15, 21.4%) and other solid tumors (n=10, 14.3%). Among the patients, the majority (61.4%) were boys. The median age was 130 months (10 years and 10 months). The median treatment time (from diagnosis to death) was 10 months. The most common cause of death was progression of the underlying disease (n=48, 69.6%), followed by TRM (n=22, 31.4%). This difference was statistically significant ($p=0.0002$). The above data are presented in [Table 1](#).

Comparative Analysis of Demographic and Clinical Characteristics of Patients with Proliferative Diseases and Solid Tumors

In both groups, the gender distribution was similar to that of the entire study population. There were more boys in both cases of proliferative diseases (60.8%) and solid tumors (57.8%). The median age of patients with proliferative diseases was 148 months, and with solid tumors – 113 months. However, this difference was not statistically significant ($p=0.3501$). The only significant difference in median age was observed in patients with Ewing's sarcoma. These patients were significantly older than the rest of the population with solid tumors (180 months [min-max: 106–203; IQR: 144.25–194.75] vs 99 months [min-max: 2–192; IQR: 28.25–138.25], $p=0.0172$). This relationship is shown in [Figure 1](#).

The median time from diagnosis to death was significantly longer in patients with solid tumors than in those with proliferative diseases (15 and 8 months, respectively, $p=0.0087$). The median survival of patients with CNS tumors was significantly shorter than that of patients with other solid tumors (10.5 vs 19.5 months, $p=0.0461$). In contrast, in patients with Ewing's tumor, this time was significantly longer (22 vs 13 months, $p=0.0248$). The above data are illustrated in [Figure 2](#).

Table 1 Descriptive Statistics of Demographic and Clinical Data

Variable	N (%) / Median (IQR) [Min-Max]
Sex	
Male	43 (61.4%)
Female	27 (38.6%)
Age [months]	130 (2–216) [41–179]
Diagnosis	
Leukemia	37 (52.9%)
ALL	22 (31.4%)
AML	15 (21.5%)
Lymphoma	7 (10.0%)
Hodgkin	1 (1.4%)
Non-Hodgkin	6 (8.6%)
MDS	2 (2.9%)
Solid tumors	24 (34.3%)
Ewing sarcoma	5 (7.1%)
Medulloblastoma	3 (4.3%)
Neuroblastoma	3 (4.3%)
Gastrointestinal	1 (1.4%)
Other CNS tumors	12 (17.1%)
Time to death [months]	10 (0.03–312) [4–17]
Reason of death	
Progression of the disease	48 (69.6%)
Treatment complications	22 (31.4%)

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; CNS, central nervous system.

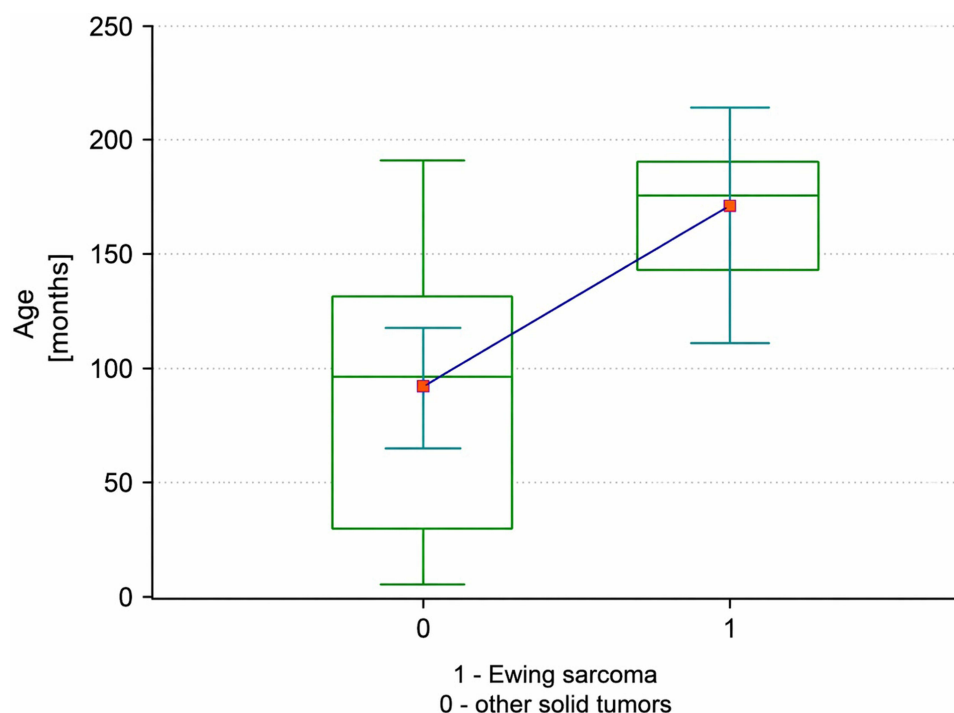


Figure 1 Median age of patients with Ewing sarcoma compared with other solid tumors.

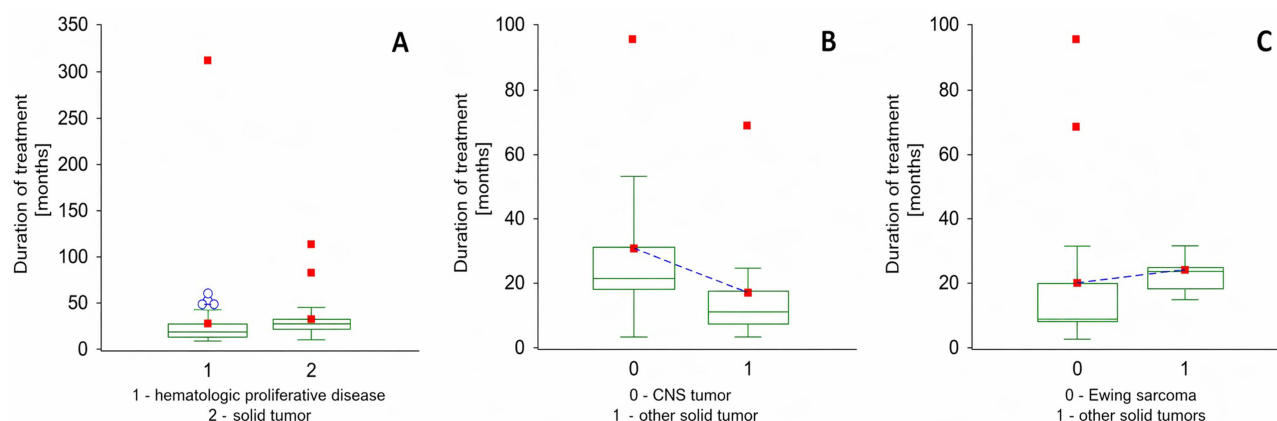


Figure 2 Median time to death in patients with (A) proliferative diseases versus solid tumors, (B) CNS tumors versus other solid tumors, and (C) Ewing sarcoma versus other solid tumors.

Patients with proliferative diseases developed hemorrhagic ($p=0.0384$) and infectious ($p=0.0418$) complications significantly more often during therapy. A similar relationship was not observed in the case of bone marrow aplasia or gastrointestinal complications. Among patients with solid tumors, the occurrence of fever at the time of diagnosis was a significant risk factor for aplasia as a complication of subsequent chemotherapy ($AUC=0.709$, $p=0.0171$; Figure 3). A similar relationship was not observed for other complications and symptoms in any of the groups. In laboratory results at admission, patients with solid tumors had significantly higher platelet counts (301 vs 96 G/L, $p=0.0093$), neutrophils (3900 vs 1775 G/L, $p=0.0227$) and lower hemoglobin (11.95 vs 9.5 g/dl, $p=0.0016$). Interestingly, differences in lactate dehydrogenase activity were not statistically significant. In both groups, patients most often died due to progression of the underlying disease. This percentage was significantly higher among patients with solid tumors than those with proliferative diseases (83.3% vs 50%, $p=0.0098$).

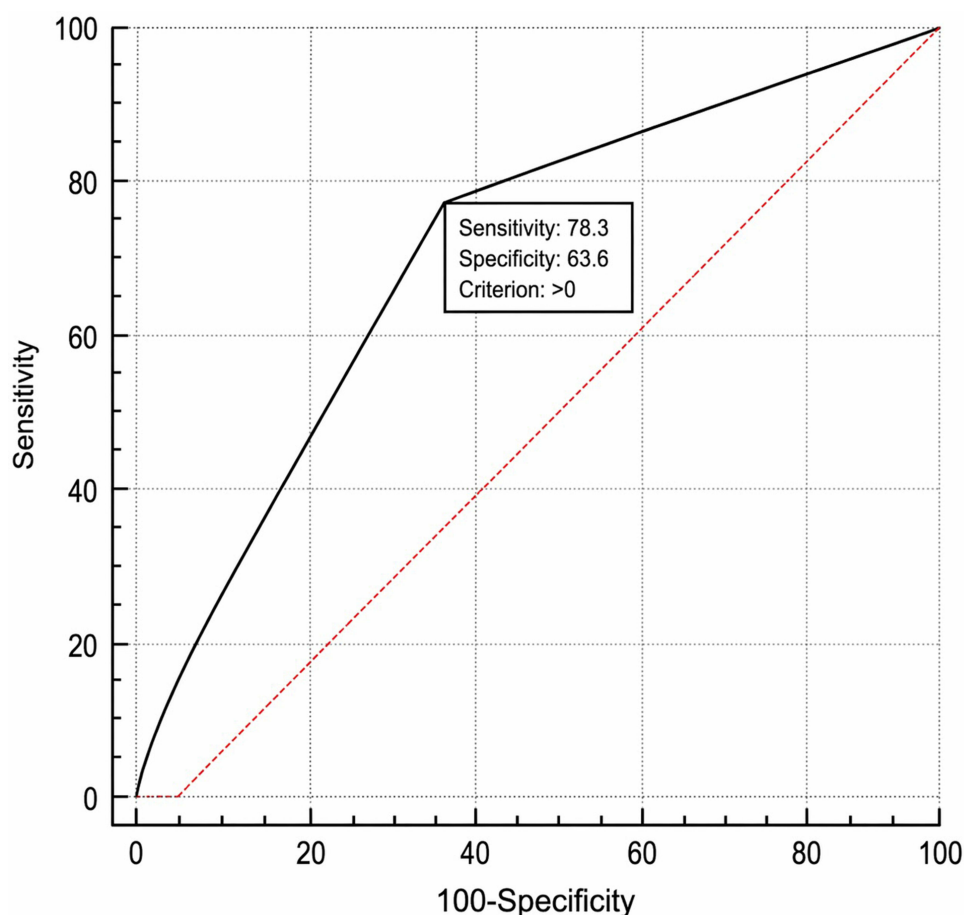


Figure 3 Fever at diagnosis as a predictor of bone marrow aplasia during chemotherapy in patients with solid tumors.

Comparative Analysis of Demographic and Clinical Data of Patients with Leukemia and Lymphoma

Differences in patient distribution based on gender and average age were not statistically significant. Survival time was significantly shorter in patients with lymphoma than in those with leukemia (7 vs 9 months, $p < 0.0001$, [Figure 4](#)). Patients diagnosed with leukemia developed hemorrhagic complications significantly more often than patients with lymphoma ($p = 0.0384$). Patients with leukemia had significantly higher lymphocyte levels (2.43 vs 0.99 G/L, $p < 0.0001$) and lower platelet levels (75 vs 319 G/L, $p = 0.0093$) than patients with lymphoma. The above data are presented in [Table 2](#).

Interestingly, although infectious complications occurred in both groups of patients, none of the children diagnosed with lymphoma died from TRM or IRM. The deaths of these patients were caused solely by the progression of the underlying disease. Thus, a significantly higher percentage of patients with lymphoma than with leukemia died due to disease progression (100% vs 80.4%, $p = 0.0195$).

Comparative Analysis of Demographic and Clinical Characteristics of Patients with Acute Lymphoblastic Leukemia and Myeloid Leukemia

Patients with acute myeloid leukemia (AML) were significantly younger at the time of death than patients with acute lymphoblastic leukemia (ALL) (128 vs 142 months, $p = 0.0013$, [Figure 5A](#)). This group also had a significantly shorter survival time (3 vs 11.5 months, $p < 0.0001$, [Figure 5B](#)). The difference in the incidence of complications between the two groups was not statistically significant for any complication. An interesting observation is that the only statistically

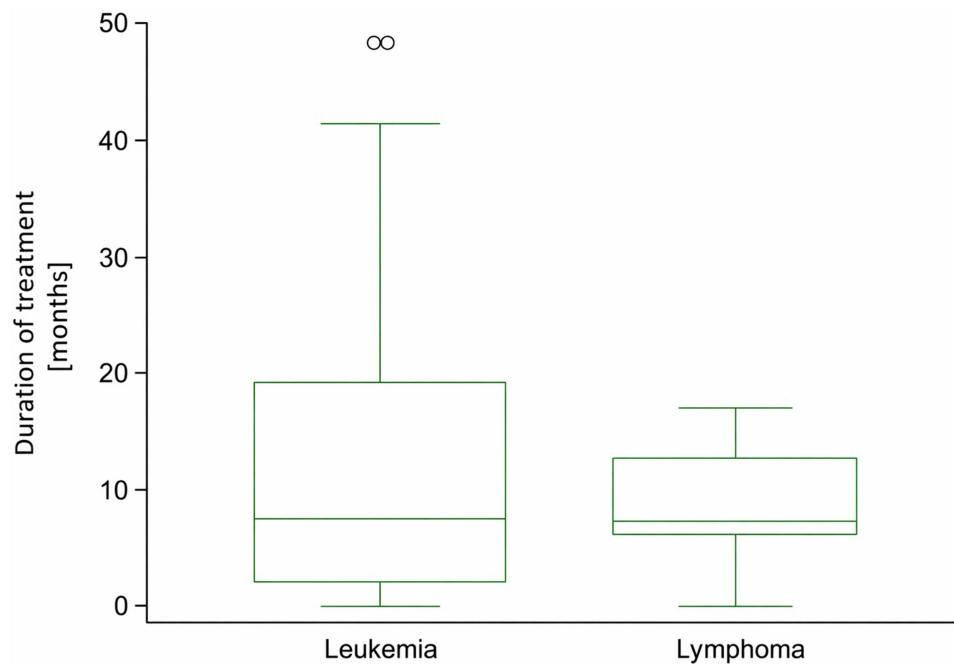


Figure 4 Median time to death in patients with leukemias versus lymphomas.

significant difference in laboratory test results between ALL and AML was LDH activity (737 vs 506, $p < 0.0001$). The above data are presented in Table 3.

Among the causes of death for both ALL and AML patients, the most common was progression of the underlying disease (81.8% and 60%, respectively, $p = 0.1555$). TRM therefore accounted for a higher percentage among AML patients, although this difference was not statistically significant.

Table 2 Comparison of Clinical and Demographic Characteristics of Deceased Patients with Leukemia or Lymphoma

Variable	Leukemia (N=37; 77.1%)	Lymphoma (N=7; 14.6%)	p
Sex			0.6919
Male	22 (59.5%)	5 (71.4%)	
Female	15 (40.5%)	2 (28.6%)	
Age [months]	132 (39.8–173.2) [13–216]	182 (80–193) [17–207]	0.5170
Time to death [months]	9 (2–18.8) [0.03–48]	7 (6.3–12.5) [0.16–17]	<0.0001*
Reason of death			0.0522
Progression	21 (56.8%)	7 (100.0%)	
Treatment complications	15 (43.2%)	0	
Treatment complications			0.9827
Infection	30 (81.1%)	6 (85.7%)	
Gastrointestinal	14 (37.8%)	1 (14.3%)	0.3623
Hemorrhagic	17 (45.9%)	0	0.0384*
Aplasia	19 (51.4%)	3 (42.9%)	0.2740
LABORATORY FINDINGS			

(Continued)

**Table 2** (Continued).

Variable	Leukemia (N=37; 77.1%)	Lymphoma (N=7; 14.6%)	p
WBC [G/L]	7.61 (2.8–68.9) [0–560]	7.1 (3.6–8.6) [0.9–34.1]	0.2742
LYM [G/L]	2.43 (1.1–19.9) [0–484]	0.99 (0.6–2.9) [0.3–8.2]	<0.0001*
NEUTR [G/L]	1.77 (0.4–5.4) [0–27.9]	4.64 (1.6–5.9) [0.4–17.3]	0.2430
PLT [G/L]	75 (43–194) [15–402]	319 (247–366) [32–425]	0.0093*
HGB [g/dl]	9.6 (8.1–10.9) [2.7–13.7]	9.8 (8.6–10.9) [7.8–15.2]	0.4354
LDH [U/L]	621 (320–1146) [101–12,735]	348 (254–465) [194–552]	0.0754
CRP [mg/l]	14.93 (3.7–30.9) [0.04–62]	8.4 (6.4–13.9) [2.16–19.1]	0.3149
PCT [ng/mL]	1.62 (0.9–10) [0.1–142.8]	2.68 (1–3.6) [0.2–6.3]	0.3495
CLINICAL SYMPTOMS			
Lymphadenopathy			0.7401
Yes	18 (48.6%)	4 (57.1%)	
No	19 (51.4%)	3 (42.9%)	
Hepatosplenomegaly			0.8776
Yes	10 (27.3%)	3 (42.9%)	
No	17 (45.9%)	4 (57.1%)	
Fever			0.8776
Yes	16 (43.2%)	5 (71.4%)	
No	11 (56.8%)	2 (28.6%)	

Note: *Statistically significant result.

Abbreviations: WBC, white blood cells; LYM, lymphocytes; NEUTR, neutrophils; PLT, platelets; HGB, hemoglobin; LDH, lactate dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

Risk Factors of Death

A significant difference between the study and control groups concerned age and platelet count at diagnosis. Patients who died were significantly older (144 vs 107 months, $p=0.0236$) and had lower platelet counts at diagnosis (92 vs 278.5 G/L, $p=0.0007$) compared to patients who survived. Other demographic, clinical, and laboratory characteristics did not show significant differences between the groups. In univariate logistic regression analysis, higher age was significantly associated with a higher risk of death (OR=1.092, 95% CI: 1.019–1.170, $p=0.0128$), while higher platelet levels had a protective effect (OR=0.606, 95% CI: 0.453–0.810, $p=0.0071$). The relationships for the other factors remained statistically insignificant. In a multivariate analysis correlating age, sex, platelet count, and leukocyte count, the following were statistically significant: age (OR=1.083, 95% CI: 1.006–1.166, $p=0.0349$) and platelet count (OR=0.623, 95% CI: 0.456–0.851, $p=0.0029$) were statistically significant. This means that older age and lower platelet count are independent predictors of death among pediatric oncology patients. The above data are presented in [Figure 6A](#).

Treatment-Related Mortality

Twenty-two patients from the above group died due to TRM. This accounted for 44.4% of deaths in the group of patients with solid tumors and 13.6% in the group with proliferative diseases. Interestingly, no patient with a CNS tumor died due to TRM. The difference in the incidence of TRM between the groups of solid tumors and hematological malignancies and CNS tumors was statistically significant ($p=0.0432$ and $p=0.0096$, respectively).

Univariate analysis showed that the condition after HSCT was an independent risk factor for death due to infection (OR=3.64, 95% CI: 1.07–12.31, $p=0.038$). This observation was confirmed in a multivariate model (HSCT, diagnosis, gender, age) – OR=4.04, 95% CI: 1.04–15.61, $p=0.043$).

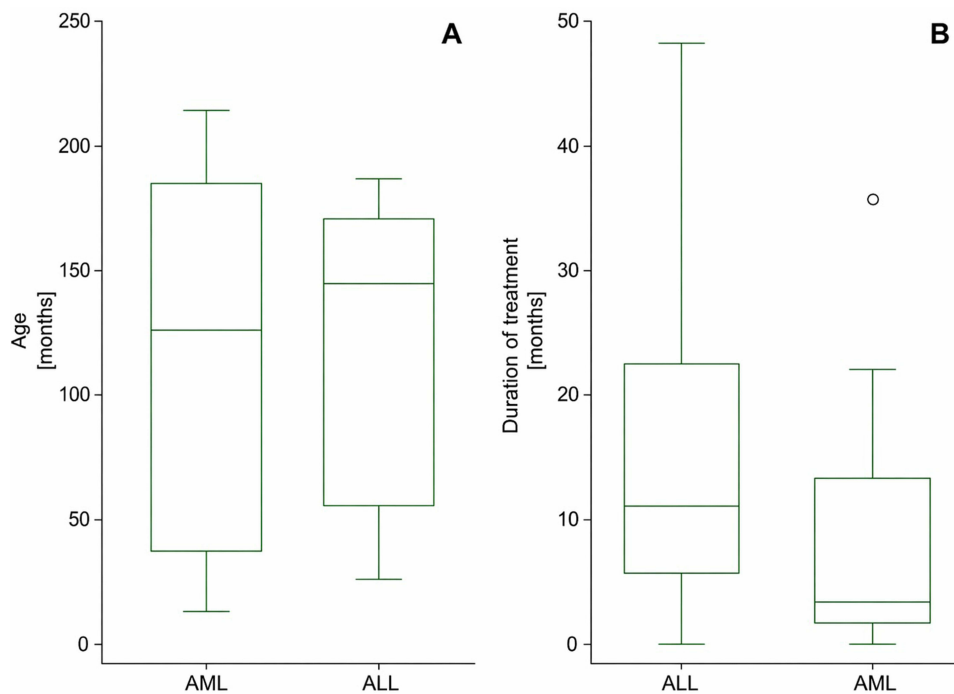


Figure 5 Comparison of patients with AML and ALL: (A) median age at death; (B) median survival time.

Factors increasing the risk of TRM in the univariate analysis were: diagnosis of a solid tumor (OR=7.2, 95% CI: 1.51–24.33, $p=0.0133$), condition after HSCT (OR=4.38, 95% CI=1.07–18.02, $p=0.040$), higher maximum procalcitonin concentration (OR=1.021 95% CI: 1.002–1.041, $p=0.027$). In the multivariate analysis, statistical significance was weakened and none of the above factors were statistically significant. The above data are presented in Figure 6B and C.

Discussion

Overall Mortality Patterns

Despite significant progress in the treatment of childhood cancers, the results obtained confirm that mortality in this population remains a significant clinical problem, and its structure depends both on the type of cancer and on complications related to treatment. In the analyzed cohort, the main cause of death was progression of the underlying disease, and TRM accounted for approximately one-third of all fatalities. Extremely similar data were presented by Pole et al in a Canadian study, describing a TRM rate of 26.4% of all deaths, and by Ramirez et al in a Mexican population (60% of deaths due to progression and 35% due to TRM).^{12,13} This pattern is typical for centers in HIC countries, where, with increasing treatment efficacy, deaths are the result of treatment resistance or disease progression.¹⁴ In LMIC countries, the percentage of TRM cases is significantly higher, even constituting the main cause of death, especially when considering infectious causes.⁸ Our results are therefore closer to the ranges expected for populations treated in European conditions, but still indicate that treatment safety and optimization of supportive care remain an important area for improvement.

Differences Between Diagnostic Groups

Although some mortality data indicate a significant proportion of patients with CNS tumors in this group, cases of leukemia mortality clearly dominated in this cohort.⁵ This may be due to the profile of our Center, where the number of patients with proliferative diseases exceeds the number of patients with solid tumors. Another aspect not observed in our hospital are cases of suicide, mainly among patients with Hodgkin's lymphoma, osteosarcoma, or germ cell tumors.¹⁵ It is worth noting that in this study, we only recorded hospital deaths. According to Gao et al, in the United Kingdom, the hospital was the most common place of death for these patients, but with an increasing incidence of mortality in

**Table 3** Comparison of Clinical and Demographic Characteristics of Deceased Patients with Leukemia

Variable	ALL (N=22; 59.5%)	AML (N=15; 40.5%)	p
Sex			0.6919
Male	12 (54.5%)	10 (66.7%)	
Female	10 (45.5%)	5 (33.3%)	
Age [months]	142 (66–173) [27–188]	128 (33–186) [13–216]	0.0013*
Time to death [months]	11.5 (6.5–24) [0.03–48]	3 (1–14.25) [0.16–36]	<0.0001*
Reason of death			0.0930
Progression	11 (50.0%)	10 (71.4%)	
Treatment complications	11 (50.0%)	4 (28.6%)	
Treatment complications			>0.05
Infection	3 (13.6%)	3 (20.0%)	
Gastrointestinal	10 (45.5%)	4 (26.7%)	
Hemorrhagic	10 (45.5%)	7 (46.7%)	
Aplasia	11 (50.0%)	8 (53.3%)	
LABORATORY FINDINGS			
WBC [G/L]	8.4 (2.6–68) [0.1–560]	4.61 (2.9–57.6) [0–257]	0.1030
LYM [G/L]	2.35 (1.2–21.3) [0.1–484]	2.43 (1.1–8.3) [0–54.2]	0.2215
NEUTR [G/L]	2.1 (0.2–5.3) [0–26]	1 (0.5–5.3) [0–27.9]	0.317
PLT [G/L]	89 (48–264) [15–402]	49 (32.5–199.5) [17.5–262]	0.0760
HGB [g/dl]	9.65 (8.4–12.2) [5.7–13.7]	9.4 (7.9–10.7) [2.7–12.1]	0.3790
LDH [U/L]	737 (402.5–1140.3) [101–12,735]	506 (299.8–1191.3) [145–3284]	<0.0001*
Blasts in bone marrow [%]	84.4 (63.9–96.2) [19–98.4]	70.4 (9.6–87.8) [2.8–94]	0.3170
CRP [mg/l]	11.34 (3.8–27.3) [0.04–62]	17.1 (3.0–31.3) [0.61–49]	0.8090
PCT [ng/mL]	1.4 (0.9–6.5) [0.24–142.8]	6.76 (0.7–43) [0.09–95]	0.9700
CLINICAL SYMPTOMS			
Lymphadenopathy			0.6650
Yes	13 (59.1%)	5 (33.3%)	
No	9 (40.9%)	10 (66.7%)	
Hepatosplenomegaly			0.8879
Yes	7 (31.8%)	3 (20%)	
No	15 (68.2%)	12 (80%)	
Fever			0.3324
Yes	9 (40.9%)	7 (46.7%)	
No	13 (59.1%)	8 (53.3%)	

Note: *Statistically significant result.

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; WBC, white blood cells; LYM, lymphocytes; NEUTR, neutrophils; PLT, platelets; HGB, hemoglobin; LDH, lactate dehydrogenase; CRP, C-reactive protein; PCT- procalcitonin.

hospices.¹⁶ In our cohort, patients with lymphoma died exclusively due to disease progression, whereas treatment-related mortality occurred only in leukemia patients. Moreover, patients with AML were younger and had shorter survival than those with ALL, suggesting a more aggressive clinical course.

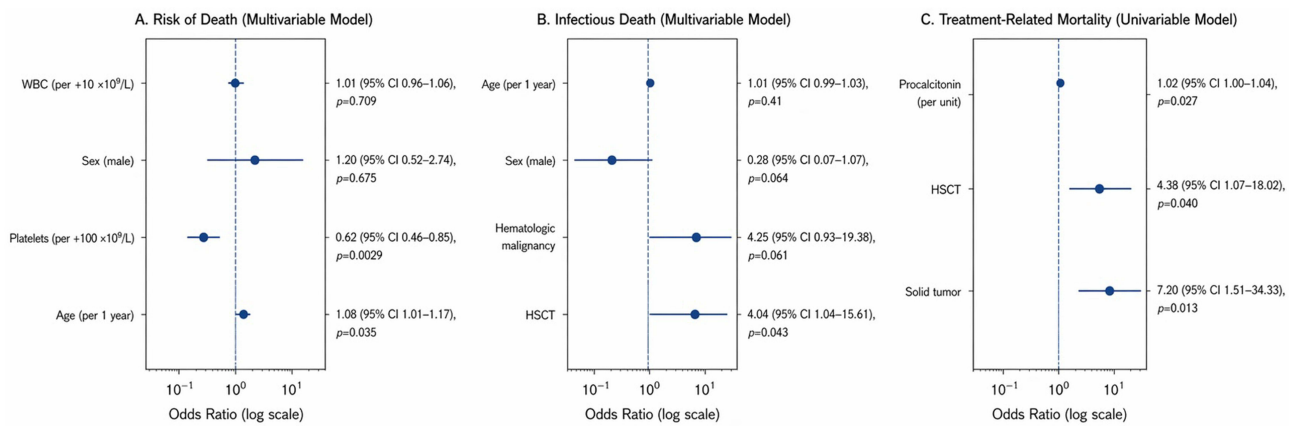


Figure 6 Regression analyses of factors associated with death and cause-specific mortality. **(A)** Multivariable logistic regression for death risk in patients with hematologic malignancies (leukemia and lymphoma) compared with controls. **(B)** Multivariable logistic regression for infectious death among deceased patients. **(C)** Univariable logistic regression for treatment-related mortality (TRM) among deceased patients.

Risk Factors for Overall Mortality

Among the risk factors for death in hospital, Gao et al noted older age and hematological cancer, which confirms our observations.¹⁶ According to Hoe et al, deaths of patients with ALL most often occurred in boys in the maintenance phase of remission. This would be consistent with our results, as the median of 11.5 months usually falls within the maintenance phase of remission.¹⁷ Another risk factor for death that we found was low platelet count. Pang et al observed that low platelet count was a risk factor for death from any cause (OR=0.83) in a pediatric intensive care unit.¹⁸ Gupta et al and Donadieu et al reached similar conclusions in patients with ALL.^{19,20} A low platelet count at the time of diagnosis may reflect not only the stage of cancer, but also the patient's general condition, the extent of bone marrow involvement, and hematological reserves prior to treatment. This may explain its independent prognostic value for both overall mortality and treatment-related mortality, including infections and hemorrhages.²¹ This points to the need for appropriate risk stratification in patients with baseline low platelet counts and the early implementation of antimicrobial prophylaxis in these patients.

Infectious Mortality and HSCT

Risk factors for death due to TRM included the condition after HSCT and higher procalcitonin levels. This would confirm previous observations describing HSCT as an independent factor in the development of bloodstream infections through prolonged and profound immunosuppression.^{22–24} This emphasizes the need for risk stratification in these patients and the implementation of appropriately intensive antimicrobial prophylaxis.^{8,23}

Clinical Implications

The present findings support the increasing importance of risk-adapted supportive care in pediatric oncology. Recent multicenter evidence has shown that implementation of pediatric early warning systems (PEWS) in hospitalized children with cancer significantly reduced mortality related to clinical deterioration events, highlighting the value of structured monitoring and early intervention pathways.²⁵

Baseline thrombocytopenia may represent a simple and readily available marker of increased vulnerability. In a large population-based study, platelet count abnormalities were independently associated with worse survival across multiple malignancies, suggesting that thrombocytopenia may reflect advanced disease burden, impaired marrow reserve, or systemic inflammation. In daily practice, children presenting with marked thrombocytopenia may benefit from closer laboratory reassessment, lower thresholds for transfusion support when clinically indicated, and intensified surveillance during induction or intensive chemotherapy.^{26,27}

Children undergoing hematopoietic stem cell transplantation remain a particularly high-risk subgroup. International transplant literature consistently identifies bacterial sepsis, invasive fungal infection, viral reactivation, and organ toxicity

as major contributors to early post-transplant mortality. Current recommendations emphasize rapid fever assessment, immediate microbiological diagnostics, early empiric antimicrobial therapy, and individualized anti-infective prophylaxis in these patients.²⁸

Older children and adolescents may also require enhanced attention. Several contemporary pediatric oncology reports describe worse outcomes in adolescents and young adults, partly related to delayed diagnosis, adverse disease biology, treatment toxicity, and lower adherence to prolonged therapy. Multidisciplinary support, including psychosocial and adherence-focused interventions, may therefore be especially relevant in this population.^{29,30}

Taken together, simple variables available at diagnosis or during treatment may help institutions implement pragmatic risk-adapted supportive care pathways while awaiting prospective validation.

Limitations of the Study

The main limitations of the study include its retrospective nature, single-center design, and limited size of individual diagnostic subgroups, which may have affected the power of multivariate analyses. In addition, the analysis included only in-hospital deaths, which may lead to an underestimation of overall mortality. Changes in treatment protocols, supportive care standards, antimicrobial strategies, and transplantation practices over the 20-year study period may have influenced mortality patterns.

Conclusions

Deaths among children with cancer remain a clinically significant problem, particularly in the context of treatment-related mortality (TRM), including infectious mortality (IRM). Older age and lower platelet count at diagnosis were identified as independent predictors of death, while post-hematopoietic stem cell transplantation (HSCT) status was associated with a higher risk of infectious death. These findings support the use of simple risk stratification at admission and during treatment. Identifying patients with older age, marked thrombocytopenia, or post-HSCT status for intensified monitoring, earlier antimicrobial prophylaxis, rapid fever-response pathways, and enhanced supportive care. Such targeted preventive strategies may help reduce avoidable mortality in high-risk pediatric oncology patients.

Data Sharing Statement

All data are available in the manuscript. Additional data are available from the corresponding author upon request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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