

Pediatric cancers in Tunisia: Epidemiology, clinical characteristics and survival outcomes from a 10-year single-center experience

Cancers de l'enfant en Tunisie: Profil épidémiologique, caractéristiques cliniques et résultats de survie d'une expérience monocentrique sur 10 ans

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ABSTRACT

Background and aims: Pediatric cancers represent a major public health challenge, particularly in low- and middle-income countries (LMICs). This study aimed to describe the epidemiological and clinical characteristics of pediatric cancers managed at a reference center in Tunisia, analyze treatment pathways, and identify prognostic factors associated with net survival.

Methods: A retrospective, single-center, observational prognostic study was conducted at the Pediatric Oncology Unit (POU) of Béchir Hamza Children's Hospital of Tunis over ten years (January 2012 – December 2021), in accordance with STROBE guidelines. All children diagnosed with cancer before age 16 years were included.

Results: A total of 563 children were included (sex ratio 1.18). Mean age at diagnosis was 4.3 ± 3.8 years (median: 3.0 years). Solid tumors predominated (81%), led by neuroblastoma (23.6%), renal tumors (17.2%), and retinoblastoma (10.7%). Five-year net survival was 69%. Multivariate Cox regression identified four independent prognostic factors: leukemia (HR=3.33, 95% CI: 2.07–5.35, $p<0.001$), metastatic disease (HR=2.65, 95% CI: 1.92–3.66, $p<0.001$), relapse (HR=2.74, 95% CI: 1.96–3.82, $p<0.001$), and residence >100 km from the POU (HR=1.32, 95% CI: 0.97–1.80, $p=0.018$).

Conclusions: Satisfactory survival outcomes are achievable in resource-limited settings with a well-structured oncology unit. Reducing geographic barriers to care and strengthening early diagnosis remain key priorities to further improve outcomes.

Keywords: pediatric cancer; net survival; epidemiology; prognostic factors; Tunisia; low- and middle-income countries

RÉSUMÉ

Contexte : Les cancers pédiatriques restent une préoccupation majeure de santé publique dans le monde, avec des disparités marquées de survie entre les pays à revenu élevé et les pays à revenu faible et moyen (PRPIC). En Tunisie, l'absence d'un registre national du cancer pédiatrique limite la connaissance de l'épidémiologie et des résultats.

Objectif : Décrire les caractéristiques épidémiologiques et cliniques des cancers pédiatriques pris en charge dans un centre de référence national en Tunisie et identifier les facteurs pronostiques associés à la survie.

Méthodes : Nous avons mené une étude observationnelle rétrospective incluant tous les enfants diagnostiqués atteints d'un cancer avant l'âge de 16 ans et traités à l'unité d'oncologie pédiatrique de l'hôpital pour enfants Béchir Hamza de Tunis entre 2012 et 2021. Des données épidémiologiques, cliniques, thérapeutiques et issues ont été collectées. Les résultats de survie ont été analysés à l'aide d'estimations de Kaplan-Meier. Les facteurs pronostiques ont été évalués à l'aide de tests de rang logarithmique univariés et de régression des risques proportionnels de Cox multivariée.

Résultats : Un total de 563 enfants ont été inclus (âge médian : 3 ans ; ratio de sexe : 1,18). Les tumeurs solides représentaient 81 % des cas, principalement un neuroblastome et des tumeurs rénales. La maladie métastatique était présente au diagnostic chez 29 % des patients. Après un suivi médian de 44 mois, la survie nette à 2 et 5 ans était de 76 % et 69 %. Les prédicteurs indépendants d'une survie plus faible étaient la leucémie, la maladie métastatique au diagnostic, la rechute et la résidence à plus de 100 km de l'unité d'oncologie.

Conclusion : Malgré les limites de ressources, des résultats de survie satisfaisants peuvent être atteints dans une unité structurée d'oncologie pédiatrique en Tunisie. Un diagnostic précoce, un meilleur accès géographique aux soins et l'élaboration de registres nationaux du cancer pédiatrique sont essentiels pour améliorer davantage les résultats.

Mots clés : Cancer pédiatrique, tumeurs solides, Épidémiologie, Survie, Registre, Diagnostic précoce, Résultat, Retard diagnostique

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INTRODUCTION

Pediatric cancers represent a major public health challenge worldwide, with significant diagnostic and therapeutic difficulties. They constitute the second leading cause of mortality among children, with an estimated 400,000 new cases diagnosed annually in patients aged 0–19 years (1). Over recent decades, advances in pediatric oncology have resulted in substantial improvements in survival. However, marked disparities persist between high-income countries (HIC) and low-middle-income countries (LMICs) (1). In LMICs, limited access to specialized pediatric oncology services, shortages of trained healthcare professionals, and restricted diagnostic and therapeutic resources contribute significantly to poorer outcomes. In addition, preventable causes of mortality including delayed diagnosis, treatment abandonment, and disease relapse remain frequent challenges. In Tunisia, the absence of a national pediatric cancer registry and the scarcity of consistently published epidemiological data hinder accurate estimation of disease burden, cancer distribution, and survival outcomes among children. Conducted at the Children's Béchir Hamza Hospital of Tunis, one of the main pilot pediatric oncology units in the capital city, this study aimed to describe the epidemiological and clinical characteristics of pediatric cancers managed in this center, analyze treatment pathways, and identify prognostic factors associated with net survival.

METHODS

Study Design and Reporting Guidelines

We conducted a retrospective observational prognostic study at the Pediatric Oncology Unit (POU) of the Department of Pediatrics A, Béchir Hamza Children's Hospital of Tunis, a national reference center for pediatric cancer care. This study is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Ethical Considerations

The study protocol was approved by the local Ethics Committee of Béchir Hamza Children's Hospital. Confidentiality and anonymity of patient data were strictly maintained throughout the study, in accordance with the Declaration of Helsinki.

Study Population

All children diagnosed with cancer before the age of 16 years and treated in the POU between 1 January 2012 and 31 December 2021 were included. Patients were excluded if medical records were unavailable or insufficiently documented, if treatment was abandoned during the initial diagnostic work-up before therapy initiation, or if death occurred before diagnostic confirmation.

Data Collection

Data were retrospectively extracted from admission registries and individual medical records using a standardized electronic data-collection form. Collected variables included epidemiological, clinical, therapeutic, and outcome data.

Epidemiological variables

Age at diagnosis, sex, region of residence, distance from home to the POU, school level (children >6 years), parental education, parental consanguinity, and socioeconomic status were recorded.

Clinical Variables

Clinical data included personal or family history of cancer or cancer-predisposing syndromes, age at symptom onset, diagnostic delay (defined as the interval between first symptom onset and histological or biological diagnostic confirmation; a cut-off of 4 weeks was used to classify delays as short [≤ 4 weeks] or prolonged [> 4 weeks], consistent with published paediatric oncology literature), and presenting symptoms. Cancer type was classified according to the International Classification of Childhood Cancer (ICCC, ICD-O-3/WHO 2008), tumor site, diagnostic confirmation method, and disease stage (localized vs metastatic).

Treatment and follow-up

Treatment modalities included surgery, chemotherapy, radiotherapy, and high-dose chemotherapy followed by autologous hematopoietic stem-cell transplantation when indicated. OS was defined as the time from diagnostic confirmation to death from any cause or last known contact (LKC). Net survival was defined as the time from diagnosis to death attributable to cancer. Relapse-free survival (RFS) was defined as the time from diagnosis to relapse, death, or LKC.

Tumor response was classified as Complete remission (CR) in case of no evidence of disease, partial remission (PR) if there is $\geq 50\%$ reduction in tumor burden, progressive disease (PD) in case of absence of response or further progression despite therapy and relapse in case of reappearance of disease at the primary site or any metastatic site after CR. For deceased patients, we documented the cause of death and the interval between diagnosis and death.

Statistical Analysis

Data were entered and analyzed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY). Qualitative variables were summarized as absolute numbers and percentages. Quantitative variables were described using means $\pm$ standard deviation, medians with interquartile range (IQR), and range when appropriate. Statistical significance was set at $p < 0.05$. Associations between quantitative variables were examined using

Pearson correlation or Spearman's rank coefficient if normality assumptions were not met. Comparisons of means used Student's t-test (two groups) or ANOVA (>2 groups) and comparisons of proportions used Pearson's chi-square test or Fisher's exact test when applicable.

RESULTS

A total of 563 children were included. The mean number of newly diagnosed patients was 56 per year (range: 50–62). The cohort consisted of 305 boys (54%) and 258 girls (46%), giving a sex ratio of 1.18. The mean age at diagnosis was 4.3 ± 3.8 years (median: 3.0 years, IQR: 1.4–5.9; range: 0–16.3 years), with the 1–4-year age group representing the majority (54%) (Figure 1).

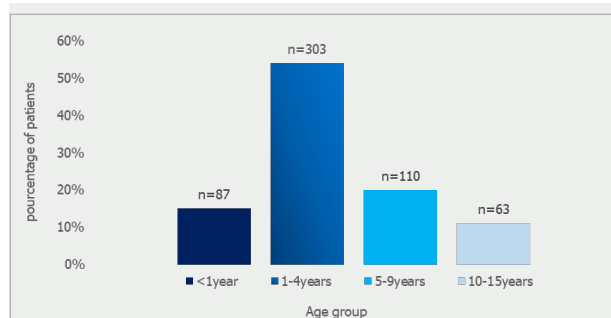


Figure 1. Patients distribution according to age

Family history showed parental consanguinity in 22% of cases, a personal or familial history of cancer in 16% (n=88), and a genetic predisposition syndrome in 2.3% of cases (n=13 patients; 21 syndrome diagnoses in total, as some patients harboured more than one condition). The most frequent syndromes were neurofibromatosis type 1 (n=8), heritable retinoblastoma predisposition (n=4), followed by other rarer conditions such as Denys–Drash (n=2), Li–Fraumeni (n=1), ataxia–telangiectasia (n=1), Bloom syndrome (n=1), Lynch syndrome (n=1), Gorlin syndrome (n=1), Peutz–Jeghers syndrome (n=1), and Down syndrome (n=1).

Three-quarters of patients sought medical attention within one week of symptom onset, while 18% of parents initially underestimated symptoms. Diagnostic errors occurred at first consultation in one-third of cases. Diagnostic delay correlated significantly with parental negligence and initial diagnostic errors, individually or combined ($p < 0.001$; Table I).

Table 1. Correlations between time to cancer diagnosis and factors contributing to diagnostic delay

Diagnostic delay factor		Median diagnostic delay (weeks)		p
Neglecting symptoms	Yes	12		<0,001
	No	4		
Misdiagnosis	Yes	7		<0,001
	No	3		
Initial clinical severity	Yes	6		0,93
	No	4		

Median diagnostic delay also varied significantly by age group and was longer in older children (10–15 years): 7 weeks versus 3 weeks for infants under 1 year ($p = 0.04$). The median diagnostic interval was 4 weeks (IQR 2–9). Shortest delays (≤ 2 weeks) were observed in hepatoblastoma, Wilms tumor, leukemias, and malignant germ cell tumors. Longest delays (≥ 10 weeks) occurred in Central Nervous System (CNS) tumors, epithelial tumors, and Ewing sarcoma.

Clinical presentation

The most common presenting features were focal signs (76%, n=431), mainly palpable masses or tumor-related compression. Less frequently, cancers were revealed by general symptoms (6%, n=33), metastatic signs (4%, n=22), or incidentally (10%, n=59).

Solid tumors accounted for the majority (n=456, 81%) and were dominated by neuroblastoma (23.6%, n=133), renal tumors (17.2%, n=97) including Wilms tumor (15.1%, n=85), retinoblastoma (10.7%, n=60), soft-tissue sarcomas (9.6%, n=54), lymphomas (9.9%, n=56). The other types were bone tumors (7.3%, n=41), CNS tumors (5%, n=28), leukemias (5.2%, n=29), and malignant germ cell tumors (4.1%, n=23) (Figure 2).

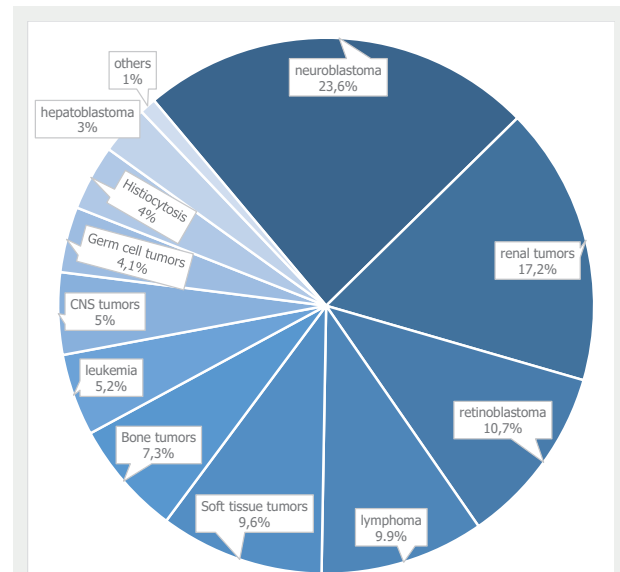


Figure 2. Distribution of cancers according to the International Classification of Childhood Cancer. Abbreviation :Central Nervous System : CNS

At diagnosis, 31% (n=175) of cancers were metastatic. The main metastatic sites were bone (n=63, 36%), bone marrow (n=60, 34%), lungs (n=51, 29%), lymph nodes (n=38, 22%), and liver (n=28, 16%). High metastatic rates were observed in neuroblastoma (51%, n=68/133), malignant germ cell tumors (43%, n=10/23), and bone tumors (41%, n=17/41).

Treatment

Chemotherapy was initiated in 96% of patients, surgery was performed in 80% of solid tumors, and one-quarter of patients received curative radiotherapy, mainly for

Hodgkin lymphoma (n=19), soft-tissue sarcomas (n= 33), Ewing sarcoma (n=11) and CNS tumors (n=9). High-dose chemotherapy with autologous stem cell transplantation was performed to 36 patients, predominantly those with high-risk neuroblastoma (n=32).

Outcomes

After a mean follow-up of 44 ± 34 months (range 0–126), 168 deaths were recorded (mortality rate 30%). Most deaths (82%) occurred within two years of diagnosis. Causes included tumor progression (77%) and chemotherapy-related toxicity (17%). The tumors most frequently associated with death were neuroblastoma, soft-tissue sarcomas, leukemias, and bone tumors. Among survivors, the mean follow-up was 62 ± 32 months, with a median of 54 months.

During follow-up, 13% of patients (n=75) relapsed after a mean of 21 ± 15 months, and 1% (n=4) developed a second malignant neoplasm. Loss to follow-up was low (3.6%, n=20). This rate decreased over time, from 6% during the 2012–2016 period to 2% during the 2017–2021 period.

Half of all deaths, regardless of cause, occurred within one year of diagnosis, and 80% of deaths attributed to cancer occurred within the first two years following diagnosis (Figure 3).

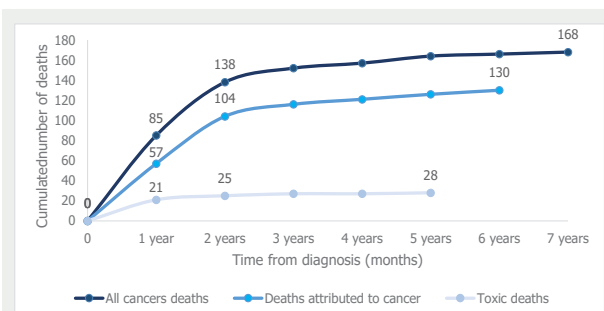


Figure 3. Time to death in relation to the date of cancer diagnosis

Survival analysis

According to Kaplan–Meier estimates, OS was 75% at 2 years, 67% at 5 years and the net survival was 76% at 2 years, 69% at 5 years (Figure 4).

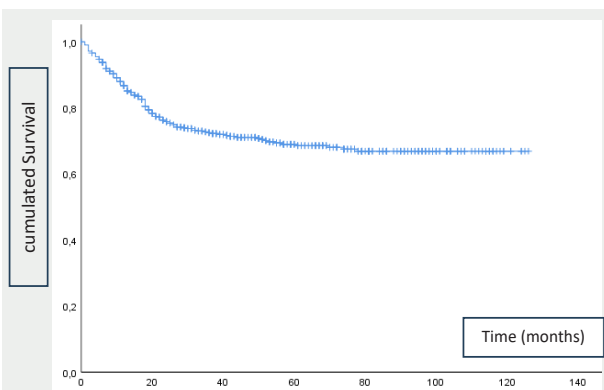


Figure 4. Overall survival of patients

Univariate analysis (Log-Rank test) identified several factors of survival (table II): age at diagnosis ($p=0.035$), distance from residence to the oncology unit ($p=0.001$), diagnostic errors ($p=0.012$), clinical presentation ($p < 0.001$), diagnostic delay ($p=0.017$), tumor type ($p < 0.001$), tumor site ($p < 0.001$), nodal extension ($p=0.005$), metastatic disease ($p < 0.001$), and relapse ($p < 0.001$).

Table 2. Correlations between 5-year net survival and prognostic factors in univariate analysis

Variable		5-year net Survival	p
Age at diagnosis	≤ 2 years	77%	0.035
	> 2 years	65%	
Sex	Male	69%	0.876
	female	69%	
Distance residence-POU	≤ 100 km	73%	0.001
	> 100 km	62%	
Socio-economic status	Low	81%	0.216
	average	72%	
	high	64%	
Diagnostic error	No	74%	0.012
	yes	61%	
Presentation mode	Focal signs	82%	<0.001
	Metastases	47%	
	Focal signs+ Metastases	21%	
	Deterioration of general condition	42%	
	Paraneoplastic syndrome	100%	
Diagnostic delay	≤ 2 weeks	77%	0.017
	> 2 weeks	65%	
Type of cancer			<0.001
	Germ cell tumors	89%	
	Renal tumors	87%	
	Soft tissue tumors	50%	
	leukemias	25%	
	Epithelial Tumors	0%	
Nodal extension	N-	73%	0.005
	N+	63%	
Metastases	M-	79%	<0.001
	M+	48%	
Relapse	No	76%	<0.001
	Yes	30%	

POU: Pediatric Oncology Unit; N-: node negative; N+: node-positive; M-: no distant metastasis; M+: metastatic disease.

Multivariate Cox regression identified the following independent predictors of poorer net survival: leukemia (5-year net survival: 25%, $\beta=1.202$, HR=3.33, 95% CI: 2.07–5.35, $p<0.001$), predominantly high-risk subtypes (T-cell ALL, infant ALL); metastatic disease at diagnosis (5-year net survival: 48%, $\beta=0.974$, HR=2.65, 95% CI: 1.92–3.66, $p<0.001$), relapse (5-year net survival: 30%, $\beta=1.007$, HR=2.74, 95% CI: 1.96–3.82, $p<0.001$), and residence >100 km from the POU (5-year net survival:

62%, $\beta=0.278$, $HR=1.32$, 95% CI: 0.97–1.80, $p=0.018$). Note: the confidence interval marginally crosses 1 due to rounding, but the Wald test p -value indicates statistical significance at the 0.05 threshold).

DISCUSSION

Our study provides a comprehensive overview of the epidemiology, clinical presentation, treatment, and outcomes of pediatric cancers managed at the POU of Béchir Hamza Children's Hospital of Tunis over a ten-year period, offering critical insights for the management of pediatric cancers in LMICs.

Incidence

In 2020, approximately 200,000 new cases of paediatric cancer were recorded worldwide, with a higher incidence in regions with a high Human Development Index (HDI), particularly North America, Western Europe, Australia and New Zealand, compared to a lower incidence in regions with low HDI (2), which could be attributed to underdiagnosis in these countries (3). Tunisia is one of the countries that does not have a specific cancer registry dedicated to children. Nevertheless, according to the North Tunisia Cancer Registry, a total of 591 cases of cancer in children were recorded during the period 2010–2014, representing 1.4% of all cancers (1.6% in boys and 1.3% in girls). The standardised incidence rate was 12.0/100,000 in males and 8.6/100,000 in females (4). According to Central Tunisia Cancer Registry, 727 cases were recorded in the center of Tunisia between 1993 and 2006, representing an annual incidence of 52 cases (5).

The predominance of young children in our study (median age 3 years, 54% aged 1–4 years) and the slight male predominance (sex ratio 1.18) are consistent with previous pediatric oncology reports worldwide (6). Familial consanguinity (22%), personal/family cancer history (16%), and identified cancer predisposition syndromes (2.3%, $n=13$) underscore the relevance of genetic factors in this population, consistent with reports from other LMICs (7).

In our study, the main mode of presentation was either signs of tumour compression or a palpable mass in three-quarters of patients. More rarely, tumours were revealed by deterioration of general condition (6%), mainly in leukaemia, or by signs related to metastatic sites (4%). The symptoms of cancer are often non-specific, insidious and can mimic the signs of common paediatric conditions (8). In general, functional signs depend on the histological type of tumour, its location, size and distant spread. Warning signs that should alert practitioners include any persistent and unexplained symptoms, bone or rheumatic pain, general signs such as prolonged fever, a palpable mass, visceromegaly, or polyadenopathy.

Diagnostic pathways and delays

In our cohort, three-quarters of patients sought care

promptly, yet 18% of parents initially underestimated symptoms, and diagnostic errors occurred in one-third of cases. Median diagnostic delay was 4 weeks, with longer delays in older children and CNS or epithelial tumors and a significant correlation ($p<0.001$) between diagnostic delay and neglect of symptoms and/or diagnostic errors. Our results are consistent with the literature. In fact, systematic reviews of the literature have concluded that certain factors correlate positively with the time to diagnosis of paediatric cancers, namely the non-specific nature of symptoms, the advanced age of the child, the specialisation of the first doctor consulted, the histological type of tumour and its location. The shortest delays were observed in leukaemia, Wilms tumor and non-Hodgkin's lymphoma, while Ewing's sarcoma and brain tumours were diagnosed after a longer delay. This difference is mainly attributable to tumor growth dynamics, with progression rates varying according to the type of cancer (9).

Tumor spectrum and clinical presentation

In our study, solid tumors dominated (81%), with neuroblastoma, renal tumors, retinoblastoma, soft-tissue sarcomas, and lymphomas being most frequent. CNS tumors and leukemias were less prevalent, reflecting patterns reported in regional registries. The population-based registry study by Steliarova-Foucher et al examined the incidence of different types of childhood cancer worldwide during the decade 2001–2010 (3). The results showed that the most common cancers in children aged 0 to 14 years, across all regions, were leukaemia, CNS tumours and lymphomas, respectively. The relatively low proportion of leukemias and CNS tumors in our cohort reflects referral patterns, as only infant leukemias and CNS tumors requiring adjuvant chemotherapy are managed in our unit.

Regarding the extension, metastatic disease was present in 29% at diagnosis, predominantly in bone, bone marrow, lungs, lymph nodes, and liver, with the highest metastatic potential in neuroblastomas, malignant germ cell tumors, and bone tumors. These results are consistent with the literature since it is reported that approximately one quarter of children with solid tumours are treated at a metastatic stage, and approximately one in five patients initially presenting with a localised tumour will develop metastases during the course of the disease (10).

Survival outcomes

Despite being a resource-limited setting, survival outcomes were satisfactory: 2- and 5-year OS were 75% and 67%, respectively, and net survival was 76% and 69%. These rates are markedly higher than those reported in many LMIC centers, where 5-year OS often falls below 40%. Worldwide, the survival rate of children with cancer varies greatly depending on the socio-economic level of each region. While the five-year OS rate is over 80% in HIC, in most LMIC, it is barely above 30% (1). According to a simulation model by Ward et al. assessing OS in pediatric cancers (11), we observed that the OS rates in our study,

across all tumor types, were substantially higher than those estimated for Africa. However, our results remain close to those of certain North African countries such as Morocco 63% (12) and Egypt 72% (13).

In our series, 3.6% of patients were lost to follow-up ($n=20$) and this rate decreased over time, from 6% of patients during the 2012-2016 period to 2% during the 2017-2021 period. There are many reasons that may explain lost to follow-up, including poor socio-economic conditions, difficulty accessing specialised oncology care facilities, negative perceptions of the disease, and a lack of psychological support throughout the course of treatment (14). These factors are all present in countries with low HDI, which explains the high rate of children lost to follow-up reported in several series, unlike in developed countries where these constraints are few or virtually non-existent, and where the challenge is rather one of providing high-quality long-term follow-up to detect delayed side effects of treatment (15). For example, the frequency of patients lost to follow-up was 26% and 34% respectively in Mali (14) and Burkina Faso (16), and exceeded 50% in East Africa (17). In contrast, this frequency was 6.6% in France (18) and 11% in Kuwait (19).

Relapse and long-term follow-up

Relapse occurred in 13% of patients after a mean of 21 months, and secondary malignancies were rare (1%). These rates are comparable to international benchmarks and suggest that disease control is achievable with current management strategies (20). The median follow-up of surviving patients (54 months) indicates a robust surveillance system, further strengthening outcome reliability.

Prognostic factors

Multivariate analysis identified leukemia, metastatic disease, relapse, and residence >100 km from the oncology unit as independent predictors of poor survival. Geographic distance from the POU emerged as an independent prognostic factor for survival in our cohort. Children living more than 100 km from the center had significantly poorer outcomes, even after adjustment for disease-related variables. Distance likely reflects multiple barriers to care, including delayed referral, difficulties in accessing specialized services, treatment interruptions, and reduced adherence to complex therapeutic protocols requiring frequent hospital visits. In pediatric oncology, these constraints may result in delayed diagnosis, suboptimal supportive care, and increased risk of complications. All these factors identified highlight health system accessibility as critical determinant of outcome, emphasizing the need for early diagnosis and equitable access to specialized care in order to reduce geographic disparities. Beyond geographic distance, the other independent prognostic factors warrant detailed discussion. Leukemia was associated with the highest mortality risk ($HR=3.33$), likely reflecting the predominance of high-risk subtypes (T-cell ALL,

infant ALL). Metastatic disease ($HR=2.65$) and relapse ($HR=2.74$) are well-established adverse prognostic factors consistent with international literature for solid tumors. Regarding geographic distance, our findings show borderline significance ($p=0.082$) after adjustment, suggesting that its impact is partly mediated by disease-related variables. Nonetheless, improving access to specialised care remains a priority. We recommend: (1) establishing regional paediatric oncology satellites to reduce travel barriers; (2) nationwide primary care awareness campaigns for earlier cancer recognition; (3) implementing standardised, tumour type-specific referral pathways.

This study has several limitations. First, its retrospective single-center design may limit generalisability to the broader Tunisian paediatric population. Second, solid tumors are overrepresented (81%) due to the referral pattern of our center: infant leukemias and CNS tumors not requiring adjuvant chemotherapy are managed at other units, explaining the relatively low proportions of leukemias (5.2%) and CNS tumors (5.0%) compared with population-based registries. Third, the absence of a national pediatric cancer registry prevents validation of our incidence estimates at the national level. Finally, 20 patients (3.6%) were lost to follow-up, which may introduce minor bias in survival estimates, although this rate compares favourably with other LMIC series (26% in Mali, 34% in Burkina Faso).

CONCLUSION

In summary, pediatric cancers in Tunisia can be managed effectively within a well-structured oncology unit and satisfactory outcomes can be achieved even in resource-limited environments. Despite resource limitations, the unit achieved acceptable survival rates, low treatment abandonment, and minimal treatment-related mortality. Moreover, strengthening early diagnosis, access to molecular diagnostics, innovative treatments like immunotherapy and targeted therapies care will be crucial to further improve survival.

The implementation of a pediatric cancer registry should be a national priority in order to create a comprehensive database accessible to all those involved in the care of these patients. This database will improve the quality of care by enabling regular evaluation of practices and identifying training and research needs, and will meet national and international requirements for the surveillance of childhood cancers.

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