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Journal of Clinical Pediatrics

ISSN 2995-6560

Research Article

Mortality Burden Among Egyptian Children And Adolescents With Cancer: A Bare-Knuckle Fight.

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Running head: Mortality among Egyptian Children with Cancer.

Abstract

Incidence rates of pediatric cancer tend to increase over the years, putting a burden on the healthcare system, particularly in low-middle-income countries (LMICs), which may be attributed to the mortality rates. We aimed to retrospectively evaluate the frequency of deaths among children diagnosed with cancer at Ain Shams Pediatric Oncology Unit in the last 10 years and to assess possible aetiology and risk factors of fatalities. A total of 500 children and adolescents with cancer were recruited, and data were collected and analyzed regarding the demographic, clinical, and disease characteristics and death-related features, timing, and possible causes. At the time of the study, the median (IQR) age was 4.25 (2.5 – 8.0) years, with male predominance (54.4% vs 45.6%). 357 (71.5%) were alive and 143 (28.5%) were dead. Of the one hundred forty-three patients who died, 37 (25.4%) died within 30 days after diagnosis (early death), 88 (61.54%) had haematological malignancies, and 55 (38.46%) had solid tumours. The highest mortality was recorded among patients with acute lymphoblastic leukaemia (31.8%), followed by acute myeloid leukaemia. Moreover, early death was significantly higher among those with haematological malignancy (34.1%) than among patients with solid tumours (12.7%) (P=0.005). The most common cause of death among patients with haematological malignancy was infection, while among those with solid tumours was the primary disease (P=0.003). We concluded that childhood cancer mortality is relatively better than previous published Egyptian studies, but lower than international figures in developed countries.

Keywords : *Mortality; Egypt; Children; Adolescents; Cancer.*

INTRODUCTION

Children with cancer respond better to treatment, they have higher life expectancies, yet the adverse effects of their illnesses and treatment bring physical and mental morbidities [1]. The 5-year overall survival (OS) of childhood cancer is generally higher in high-income countries (HICs) compared to middle-income (MICs) and low-income countries (LICs) (80% vs 55% vs 40% respectively) [2]. Childhood cancer is a priority in Egypt due to the large numbers of children diagnosed each year, the rarity of centres providing optimal care, the insufficient resources, the delayed referral for diagnosis, and the treatment abandonment [3,4]; the 5-year OS of childhood and adolescent cancer in Egyptian Oncology centres was estimated to be around 40% [5,6].

The causes of death varied markedly between different groups of primary cancer diagnosis and were highly dependent on the time passed since diagnosis [7], early death (ED) in children with cancer may be due to intracerebral haemorrhage and infections [8]. The highest risk of ED is seen in children with acute myeloid leukaemia (AML), infant acute lymphoblastic leukaemia (ALL), hepatoblastoma, and malignant brain tumours [9].

Our main goal in this work was to describe the frequency of deaths among children diagnosed with cancer in the last 10 years and to detect causes and risk factors of deaths to improve both clinical and scientific activities to reduce mortality rates in our centre with the available resources.

MATERIALS AND METHODS

This retrospective record-based study describes data from 500 children younger than 18 years old diagnosed with solid and haematological malignancies from the database of Pediatric Hematology Oncology and Bone Marrow Transplantation Department, from 1st September 2011 to 30th September

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Received: 24-July-2025, Manuscript No. JOCP-5002 **; Editor Assigned:** 26-July-2025 **; Reviewed:** 19-Aug-2025, QC No. JOCP-5002 **; Published:** 23-Aug-2025, **DOI:** 10.52338/jocp.2025.5002
Citation: **Fatma Ebeid**. Mortality Burden among Egyptian Children and Adolescents with Cancer: A Bare-Knuckle Fight. Journal of Clinical Pediatrics. 2025 August; 12(1). doi: 10.52338/jocp.2025.5002.

2021. The study was performed after getting the approval of the Institutional Ethical Committee (FMASU MS 29 / 2021). Owing to the study design, consent was waived. The collected data included the demographic characteristics (age at the time of diagnosis, gender, residency, socioeconomic status), the disease characteristics (diagnosis, initial presentation, risk stratification, presence of metastasis, staging, treatment modalities, [chemotherapy, radiotherapy, surgery, or hematopoietic stem cell transplant (HSCT)] and response, relapse, and salvage treatment.

Data regarding death (time of death, either early or late, disease status at time of death, and cause of death, whether infection, primary disease or treatment-related mortality (TRM) or other causes). The TRM is defined as death not directly due to the cancer, which includes death from infection, bleeding, and organ dysfunction. [10] Early death (ED) is defined as death within 30 days after diagnosis of the first neoplasm. [11] While non-early death is considered for patients who die after 30 days of diagnosis.

The OS was calculated from the date of diagnosis to date of death from any cause over the study period; living patients or patients lost to follow-up were censored on the last known alive date, while event-free survival (EFS) was calculated from the date of diagnosis to the date of the event (relapse death).

Statistical Analysis

Data was analysed using the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as median, inter-quartile range (IQR), and range due to non-parametric distribution. Qualitative variables were presented as numbers and percentages. The comparison between groups regarding qualitative data was performed using the Chi-square test and/or Fisher's exact test when the expected count in any cell was less than 5. The comparison between two independent groups with quantitative data and non-parametric distribution was made by using the Mann-Whitney test. Kaplan-Meier analysis assessed the relation between OS and EFS and the other parameters studied using the Log-Rank Test. P-value was considered significant if less than 0.05.

RESULTS

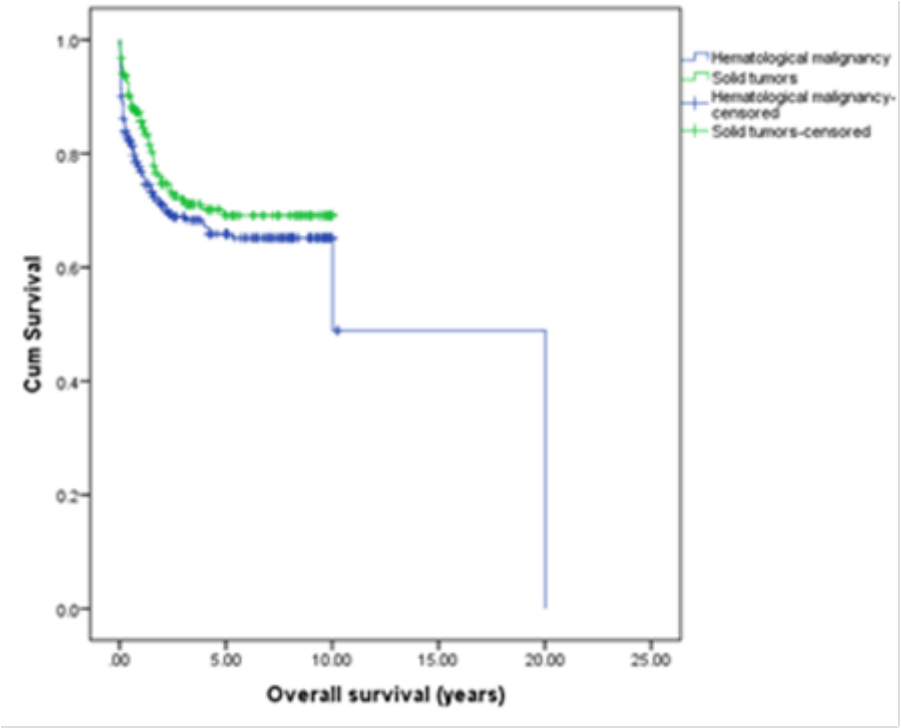
Five hundred patients were enrolled, and their median age was (IQR) 4.25 (2.5 – 8.0) years, with male predominance (54.4%). Three hundred fifty-seven were alive at the time of the study, and 143 (28.5%) were dead; among them, 37 (25.4%) died within 30 days after diagnosis (ED).

Of the 143 patients who died, 88 had haematological malignancies and 55 had solid tumours; children with ALL had the highest mortality (31.8%), followed by AML, as illustrated in **Table 1**. Moreover, ED was higher among those with haematological than solid tumours (34.1% vs 12.7%, p=0.005). The percentage of patients who relapsed was higher among cancer children who died (P=0.00). There was a non-significant effect of age, gender, the residence when comparing those alive and those who died, whether early or non-early death (P>0.05). Infection was the most common cause of death among patients with haematological malignancy (55.7% vs 34.5%), while the primary disease was the main cause of death among those with solid tumours (54.5% vs 25%, P=0.003). The 5- and 10-year OS and EFS were 67.30% and 66.90% respectively, and 72.3% and 71.7% respectively, as depicted in **Figures 1** and **2**.

Table 1. Mortality rate in different types of cancer of all studied patients with childhood malignancy over 10 years.

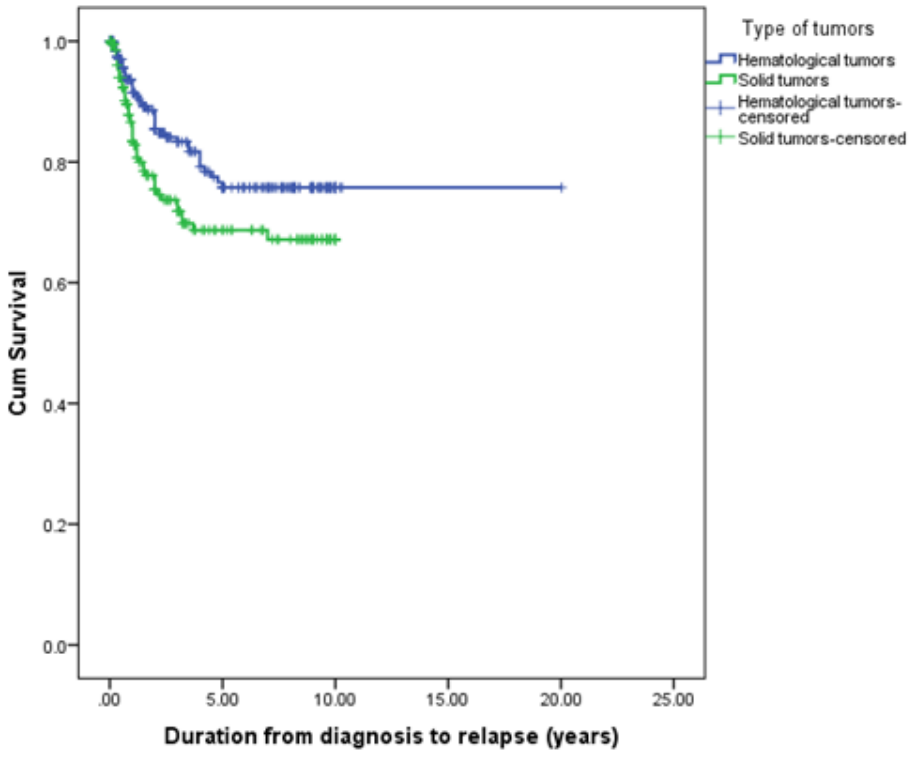
Diagnosis (n (%))	Total n=500	Total death n=143	Early death n=37	Non-early death n=106
Hematological malignancies				
Acute lymphoblastic leukemia	159 (31.8)	52 (36.4%)	17 (45.9)	35 (33.0)
Acute myeloid leukemia	73 (14.6%)	28 (19.6%)	11 (29.7)	17 (16.0)
Hodgkin and non-Hodgkin lymphoma	50 (10.0%)	8 (5.6%)	2 (5.4)	6 (5.7)
Solid Tumor				
Retinoblastoma	52 (10.4%)	9 (6.3%)	0 (0)	9 (8.5)
Neuroblastoma	51 (10.2%)	13 (9.1%)	2 (5.4)	11 (10.4)
Ewing sarcoma	17 (3.4%)	4 (2.8%)	1 (2.7)	3 (2.8)
Hepatoblastoma	7 (1.4)	3 (2.1%)	1 (2.7)	2 (1.9)
Osteosarcoma	6 (1.2%)	4 (2.8%)	0 (0)	4 (3.8)
Rhabdomyosarcoma	16 (3.2%)	7 (4.9%)	2 (5.4)	5 (4.7)
Wilms tumor	22 (4.4%)	5 (3.5%)	1 (2.7)	4 (3.8)
Brain tumors	47 (9.4%)	10 (7.0%)	0 (0)	10 (9.4)

Figure 1. Comparison between patients with haematological childhood malignancy and those with solid tumours as regards the mean overall survival of the studied patients (in years).



	Total N	N of Events	OS (years)		95% CI		Log Rank test	
			Mean	SE	Lower	Upper	X2	P-value
Hematological malignancy	282	88	11.773	1.51	8.813	14.732	2.101	0.147
Solid tumors	218	55	7.317	0.307	6.714	7.919		

Figure 2. Comparison between patients with haematological childhood malignancy and those with solid tumours as regards event-free survival.



	Total N	N of Events	PFS		95% CI		Log Rank Test	
			Mean	SE	Lower	Upper	X^2	P-value
Hematological malignancy	282	40	15.693	0.614	14.490	16.896	5.091	0.024
Solid tumors	218	49	7.252	0.334	6.598	7.906		

Acute lymphoblastic leukaemia (ALL)

Table 2 illustrates insight around death in children with ALL; relapsed ALL patients who received ALL-REZ BFM 2002 as salvage treatment showed a higher percentage of death compared to those who received FLAG or FLAG-IDA protocols (P=0.002). ALL children who died early and those who died late had a comparable frequency of cardiac and CNS complications as well as fungal infections (P=0.864, P=0.186, and P=0.442, respectively). Most ALL patients who had ED died before the end of induction (P=0.000). Infection was by far the most common cause of death in ALL patients who died early as well as those who died late (P=0.019).

Table 2. Comparison between living and dead acute lymphoblastic leukaemia (ALL) patients and those who died early and those who died late.

Variable n (%)	Alive n= 107	Dead n= 52	P-value	Early death n= 17	Non-early death n= 35	P-value
Flow cytometry (ALL)						
Pre B ALL	91 (85.0%)	42 (80.8)	0.494	11 (64.7%)	31 (88.6%)	0.041
T.cell ALL	16 (15.0%)	10 (19.2)		6 (35.3%)	4 (11.4%)	
Cytogenetic test (n%)						
Favourable	4 (3.7%)	5 (9.6)	0.188	0 (0.0%)	5 (14.3%)	0.256
Unfavorable	6 (5.6%)	5 (9.6)		2 (11.8%)	3 (8.6%)	
No identified cytogenetics	97 (90.7%)	42 (80.8)		15 (88.2%)	27 (77.1%)	
Protocol of treatment (n%)						
Total XV	62 (57.9%)	39 (75.0%)	0.036	16 (94.1%)	23 (65.7%)	0.026
CCG-1991 protocol	45 (42.1%)	13 (25.0%)		1 (5.9%)	12 (34.3%)	
Sub-classification of CCG (n%)						
Low risk	0 (0.0%)	0 (0.0%)	0.549	1 (100.0%)	5 (41.7%)	0.261
Standard risk	25 (55.6%)	6 (46.2%)		0 (0.0%)	0 (0.0%)	
High risk	20 (44.4%)	7 (53.8%)		0 (0.0%)	7 (58.3%)	
Sub-classification of total xv						
Standard risk	29 (46.8%)	17 (45.9)	0.431	6 (40.0%)	11 (50.0%)	0.363
Low risk	28 (45.2%)	14 (37.8)		5 (33.3%)	9 (40.9%)	
High risk	5 (8.1%)	6 (16.2)		4 (26.7%)	2 (9.1%)	
Response to chemotherapy at day14						
No evaluation**	0 (0.0%)	15 (28.8%)	0.000	13 (76.5%)	0 (0.0%)	0.000
Not in remission	31 (29.0%)	8 (15.4%)		1 (5.9%)	7 (20.0%)	
Remission	76 (71.0%)	29 (55.8%)		3 (17.6%)	28 (80.0%)	
Response to chemotherapy at the end of induction						
No evaluation**	0 (0.0%)	17 (32.7)	0.000	17(100.0)	0 (0.0%)	0.000
Not in remission	0 (0.0%)	0 (0.0)		0 (0.0%)	0 (0.0%)	
Remission	107 (100.0%)	35 (67.3)		0 (0.0%)	35(100.0)	
Relapse (n%)	4 (3.7%)	12 (23.1%)	0.000	0 (0)	12 (100)	NA
Type of relapse (n%)						
Medullary relapse	4 (100.0%)	8 (66.7%)	0.411			
Extra medullary relapse	0 (0.0%)	1 (8.3%)				
Both	0 (0.0%)	3 (25.0%)				

Time of relapse						
Early relapse	0 (0.0%)	8 (66.7%)	0.021			
Late relapse	4 (100.0%)	4 (33.3%)				
Protocol of relapse (n%)						
ALL-REZ BFM 2002	4 (3.7%)	6 (11.5%)	0.002			
FLAG-ida protocol	0 (0.0%)	2 (3.8%)				
FLAG protocol	0 (0.0%)	3 (5.8%)				
Disease status at time of death						
Before the end of induction				13 (76.5%)	4 (11.4%)	0.000
Remission				2 (11.8%)	18 (51.4%)	0.006
Relapse				0 (0.0%)	13 (37.1%)	0.004
Not in remission				2 (11.8%)	0 (0.0%)	0.039
Causes of death (n%)						
Infection				15 (88.2%)	16 (45.7%)	0.019
Primary malignancy				0 (0.0%)	10 (28.6%)	
Treatment related death				2 (11.8%)	6 (17.1%)	
Other causes***				0 (0.0%)	3 (8.6%)	

**no evaluation: patients died before evaluation

Acute myeloid leukemia (AML)

The percentage of deaths was significantly higher among AML patients who received the MRC12-based protocol compared to those who received the 3+7 protocol (P=0.000), as illustrated in **Table 3**. M5 and M7 AML patients represented the highest percentage among dead AML patients (P=0.048). Most AML patients who died early did not get the chance to have an evaluation done after the 2nd cycle of induction (P=0.000).

Table 3. Comparison between living and dead and early and non-early death among acute myeloid leukaemia (AML) patients as regards studied characteristics.

	Death		P-value	Time of death		P-value
	Alive	Dead		Early death	Non-early death	
	No.= 45	No.= 28		No. = 11	No.= 17	
Age (years)						
Median (IQR)	5 (2.8 – 10)	4.5 (2 – 9)	0.982	2 (2 – 5)	6 (3.5 – 12)	0.040
Range	0.25 – 15	1 – 15		1 – 11	1.5 – 15	
Gender (n%)						
Female	21 (46.7%)	19 (67.9%)	0.077	7 (63.6%)	12 (70.6%)	0.700
Male	24 (53.3%)	9 (32.1%)		4 (36.4%)	5 (29.4%)	
Subclassification (n%)						
Low risk	14 (31.1%)	7 (25.0%)	0.834	3 (27.3%)	4 (23.5%)	0.937
Standard risk	23 (51.1%)	15 (53.6%)		6 (54.5%)	9 (52.9%)	
High risk	8 (17.8%)	6 (21.4%)		2 (18.2%)	4 (23.5%)	
Cytogenetic test (n%)						
Favourable	16 (35.6%)	6 (21.4%)	0.096	2 (18.2%)	4 (23.5%)	0.333
Unfavorable	1 (2.2%)	5 (17.9%)		1 (9.1%)	4 (23.5%)	
No identified cytogenetics	24 (53.3%)	15 (53.6%)		8 (72.7%)	7 (41.2%)	
Down syndrome	4 (8.9%)	2 (7.1%)		0 (0.0%)	2 (11.8%)	

Flow cytometry (AML) (n%)						
M1	6 (13.3%)	2 (7.1%)	0.048	2 (18.2%)	0 (0.0%)	0.214
M2	14 (31.1%)	3 (10.7%)		1 (9.1%)	2 (11.8%)	
M3	8 (17.8%)	3 (10.7%)		2 (18.2%)	1 (5.9%)	
M4	5 (11.1%)	1 (3.6%)		1 (9.1%)	0 (0.0%)	
M5	9 (20.0%)	10 (35.7%)		3 (27.3%)	7 (41.2%)	
M7	5 (11.1%)	9 (32.1%)		2 (18.2%)	7 (41.2%)	
Protocol of treatment (n%)						
MRC12 based protocol	13 (28.9%)	22 (78.6%)	0.000	10 (90.9%)	12 (70.6%)	0.201
3+7 protocol	32 (71.1%)	6 (21.4%)		1 (9.1%)	5 (29.4%)	
Response to chemo after 2nd cycle of induction (n%)						
No evaluation***	0 (0.0%)	9 (32.1%)	0.000	9 (81.8%)	0 (0.0%)	0.000
Not in remission	10 (22.2%)	2 (7.1%)		2 (18.2%)	0 (0.0%)	
Remission	35 (77.8%)	17 (60.7%)		0 (0.0%)	17 (100.0%)	
Relapse (n%)	11 (24.4%)	6 (21.4%)	0.767	0 (0)	6(100)	NA
Protocol of relapse(n%)						
FLAG-ida protocol	8 (17.8%)	5 (17.9%)	0.851			
FLAG protocol	3 (6.7%)	1 (3.6%)				
Cardiac complication (n%)				1 (9.1%)	4 (23.5%)	0.330
CNS complication (n%)				1 (9.1%)	3 (17.6%)	0.527
Disease status at time of death (n%)						
Before the end of Induction (n%)				9 (81.8%)	0 (0.0%)	0.001
Remission (n%)				0 (0.0%)	11 (64.7%)	0.001
Relapse (n%)				0 (0.0%)	6 (35.3%)	0.026
Not in remission (n%)				2 (18.2%)	0 (0.0%)	0.068
Causes of death (n%)						
Infection				9 (81.8%)	7 (41.2%)	0.074
Primary malignancy				2 (18.2%)	6 (35.3%)	
Treatment-related death				0 (0.0%)	4 (23.5%)	

***no evaluation: as patients died before evaluation.

Hodgkin (HL) and non-Hodgkin lymphoma (NHL)

Two out of 20 HL were males, stage 4, treated with the ABVD protocol, died late, had complete responses after the 2nd cycle of chemotherapy, one patient died in relapse, and the other one in remission; their death was TRM. Six NHL patients died; their median age was 3.5 years, and all were males. Three patients had Burkitt's lymphoma, two had T-cell lymphoblastic lymphoma, and one had large B-cell lymphoma. Four were stage III, one was stage II, and another was stage IV. Three patients died in relapse; one patient died in remission, and two patients died early before evaluation. Two patients died of infection, two of progressive disease, and two due to treatment-related death. One patient died after autologous HSCT.

Solid Tumors

Seven children with brain tumours died in remission, and three died in relapse; their deaths were due to infection (n=4), TRM (n=3), primary disease (n=3), and autologous HSCT rescue for relapse (n=1), with a higher percentage of deaths among patients with WHO grade 4, and those with metastasis (P=0.034, P=0.002, respectively).

Twelve of 13 patients with neuroblastoma who died were high risk, and one was low risk; 10 underwent HSCT rescue. Deaths causes were primary malignancy (n=7), TRM (n=2), infection (n=1), and sudden death (n=1); with a higher rate among older children (p=0.029), those with N-myc amplification (P=0.013), those unable to have complete resection of the tumour (P=0.026), and those who relapsed (P=0.003).

Five out 9 patients with retinoblastoma who died had extraocular disease with extension to optic nerve (stage 4b (n=3) and stage 2-3 (n=2)) and four had intraocular retinoblastoma (intraocular with high-risk features (n=2), unilateral group E (n=1), bilateral group E and group B (n=1)). Five patients died of infection and four of primary malignancy. There was no significant effect on survival as regards laterality,

grouping, response to chemotherapy, the use of radiotherapy, the occurrence of relapses, and enucleation.

3 of 4 Ewing sarcoma patients who died were stage 4 (high risk), and one was stage 3 (standard risk); their main cause of death was the primary disease (n=3) and TRM (n=1). 3 of 4 osteosarcoma patients who died had metastasis and were classified as high-risk osteosarcoma, and one was standard risk; their main cause of death was TRM (n=3).

3 of 7 patients with rhabdomyosarcoma died were high-risk, three were intermediate, and one was low-risk, with the cause of death infection (n=3), primary malignancy (n=3), and TRM (n=1). Five Wilms tumour patients died; two were in stage 4 and had metastasis, two were stage 3, and one was stage 1; their deaths were due to infection (n=2), primary disease (n=2) and pulmonary embolism (n=1). 2 of 3 patients with hepatoblastoma died had mixed epithelial and mesenchymal without teratoid features and were pretext IV, and one had mixed epithelial and was pretext II. One underwent total resection, and another had radiotherapy.

DISCUSSION

Cancer care for all ages has become a global focus to improve outcomes for children and adolescents diagnosed with cancer worldwide [12]. The expected childhood cancer survival rate now exceeds 80% in countries such as the United States [13]. In our study, the 5- and 10-year OS of the studied childhood cancer were 67.30% and 66.90% respectively, while the 5- and 10-year EFS were 72.3% and 71.7% respectively. Similarly, *Leong et al*. [14] stated that the OS 5-year and 10-year rates for all childhood cancers combined were 70.0% and 68.8%, respectively. However, *González García* et al. [15] reported a higher five-year OS (84%). *Ibrahim and colleagues* [16] reported a lower OS rate (40%).

In the Eastern Mediterranean region (EMR), leukaemia was the leading cause of cancer death in all related countries, comparable with worldwide estimates and most WHO regions. Moreover, brain tumours were the second leading cause of death in most EMR countries [17]. These disparities may be caused by multiple factors, with a country's economic status being one contributor and the recent advances in pediatric oncology care [18]. In our cohort, the highest mortality was seen in ALL patients (31.8%), followed by AML (14.6%), then retinoblastoma (10.4%) and other; also we did not find a significant difference between children with haematological and solid tumours as regards the mean OS and EFS, although the percentage of childhood cancer patients who died early were significantly higher among those with hematological malignancy (34.1% vs12.7). Our findings are partially in line with *Soliman et al*. [6] who included 15,779 children with cancer across Egypt and showed that death is more prevalent among ALL (27.6%), CNS (16.9%) tumors, lymphomas (15.4%) and neuroblastoma (10%). Also, de Oliveira et al [19] illustrated that cases of leukemia (23.3%) were by far the most common cancer, followed by CNS tumors (16.9 %), and lymphoma (14.8 %). Infections are still an important cause of mortality in pediatric cancer patients [20], with mortality rates ranging from 8% to as high as 41% [21]. The main cause of death in our patients was an infection in haematological malignancies, highlighting the continuous need for strict infection control measures and hospital-based antibiotic surveillance programs. In contrast, *Loeffen et al.* [22] reported that TRM accounted for 56.3% of children with a haematological malignancy.

ALL Patients treated by the total XV protocol showed a higher frequency of death than those treated by the CCG protocol, this could be attributed to the greater intensity and toxicity related to TXV protocol, leading to a higher rate of TRM with different drug-induced toxicities in addition to a higher liability to different infectious complications attributed to prolonged immunosuppression. Furthermore, we observed higher mortality among ALL patients with CNS involvement (11.5%). In line with the current study results, *Al-Hadad et al*. [23] study in Iraq reported early deaths occurred in 6%-10% of ALL children, and *Shakibazad and Bordbar* [24] found a cumulative early mortality rate of about 4.6%. Similarly, *Noroozi* et al. [25] reported that CNS involvement in ALL had a poorer prognosis. However, among the living group, the percentage of patients who went into remission at day 14 and at the end of induction was significantly higher than those who died. In an Egyptian study, among 200 children with ALL, the induction-related deaths were 23%; a large majority of these deaths occurred at the early stages of the second re-induction, with a median survival duration of 4.5 months. Deaths were mainly due to infection-related events such as pneumonia, sepsis, or disease progression [26]. Indeed, the main cause of early death among our patients with ALL was infection (88.2%), while TRM occurred in 11.8% of patients who died early and 17.1% of non-early deaths. However, *Hafez et al*. [27] mentioned that TRM was responsible for the majority (90%) of early deaths in their cohort, and only 7% were disease-related. Bayoumi, [28] in the National Cancer Institute, Egypt, reported that infection-related mortality was in 39% of deaths, and mortality from gram-negative bacteremia was 29.9%.

In developed countries, recent advances have increased long-term survival rates to up to 65% for children with AML. However, those in LMICs have not benefited from these advances and continue to have survival rates lower than 40% [29]. In this study, AML was the second most common cause of mortality (19.6%), the main cause was infection, and TRM was reported only in non-early death in about 23.5% of the cases. Variable values for ED among AML patients were reported as 43% [27] and 11.8% [29]. In addition, *Morais et*

al. [30] reported that infection was the major cause of death in AML among (43%) and disease progression among (42%). Hodgkin lymphoma (HL) has a good prognosis [31] and reported a low mortality in the present study, which is consistent with a previous Egyptian study that reported OS was 96.6% % [32]. NHL's prognosis has improved steadily over the last two decades, with OS reaching up to 80 – 90%; however, outcomes are still inferior in LMICs. [33]. Our study revealed 6 deaths in NHL (20%); two of them died early due to infection and TRM. Mortality rate ranged from 19.7% mainly due to sepsis (47.8%) [33] to as low as 2.8% [34] with no early deaths. The best chance of cure lies in the initial diagnosis of childhood solid cancer, as well as the treatment of progression or recurrence. Nevertheless, 20%–40% of patients succumb to the disease [35]. Attempts have been made to improve the prognosis [36], but progress is lagging, probably due to the small number of patients, diversity of tumour types, and limited resources [37]. Neuroblastoma had numerous biological and genetic markers identified as prognostic markers [38]. In our study, the bad prognostic factors were older age, cases related to N-myc amplification, then relapses, and post-HSCT rescue. In LMICs, the life expectancy of retinoblastoma patients is still very low at 30% compared to >95% in HICs, with the main goals of HICs being to save the eye and maintain the best vision, while treatment in LMICs is still aimed at reducing mortality [39]. Regarding the global retinoblastoma outcome study, the mortality rate was 12.8%; 90.9% of deaths were from retinoblastoma itself [40].

CONCLUSION

Our study emphasises the need for a joint Egyptian pediatric cancer registry including all centres in Egypt, allowing a better insight into the actual death rate in childhood cancer and assessing possible causes with the development and implementation of national protocols to reduce mortality from cancer in paediatrics.

Acknowledgments

None to be acknowledged

REFERENCES

1. Shabani M, Saeedi Moghaddam S, Ataeinia B, Rezaei N, Mohebi F, Mohajer B, Gohari K, Sheidaei A, Pishgar F, Yoosefi M, Kompani F. Trends of national and subnational incidence of childhood cancer groups in Iran: 1990–2016. Frontiers in Oncology. 2020 Jan 14;9:1428.

2. Girardi F, Allemani C, Coleman MP. Worldwide trends in survival from common childhood brain tumors: a systematic review. Journal of global oncology. 2019 Nov;5:1-25.

3. Friedrich P, Lam CG, Kaur G, Itriago E, Ribeiro RC, Arora RS. Determinants of treatment abandonment in childhood cancer: results from a global survey. PloS one. 2016 Oct 13;11(10):e0163090.

4. Van Heerden J, Zaghloul M, Neven A, de Rojas T, Geel J, Patte C, Balagadde-Kambugu J, Hesseling P, Tchintseme F, Bouffet E, Hessissen L. Pediatric oncology clinical trials and collaborative research in Africa: Current landscape and future perspectives. JCO global oncology. 2020 Aug;6:1264-75.

5. Tantawy AA, El Sherif NH, Ebeid FS, El-Desouky ED. Survival analysis after diagnosis with malignancy of Egyptian adolescent patients: a single-center experience. Journal of pediatric hematology/oncology. 2014 Aug 1;36(6):e346-52.

6. Soliman RM, Elhaddad A, Oke J, Eweida W, Sidhom I, Ahmed S, Abdelrahman H, Moussa E, Fawzy M, Zamzam M, Zekri W. Temporal trends in childhood cancer survival in Egypt, 2007 to 2017: A large retrospective study of 14 808 children with cancer from the Children's Cancer Hospital Egypt. International journal of cancer. 2021 Apr 1;148(7):1562-74.

7. Yu XQ, Dasgupta P, Kahn C, Kou K, Cramb S, Baade P. Crude probability of death for cancer patients by spread of disease in New South Wales, Australia 1985 to 2014. Cancer Medicine. 2021 Jun;10(11):3524-32.

8. Caballero M, Faura A, Margarit A, Bobillo-Perez S, Català A, Alonso-Saladrigues A, Conde N, Balaguer M, Rives S, Jordan I. Outcomes for paediatric acute leukaemia patients admitted to the paediatric intensive care unit. European Journal of Pediatrics. 2022 Mar 1:1-9.

9. Green DM, Kun LE, Matthay KK, Meadows AT, Meyer WH, Meyers PA, Spunt SL, Robison LL, Hudson MM. Relevance of historical therapeutic approaches to the contemporary treatment of pediatric solid tumors. Pediatric blood & cancer. 2013 Jul;60(7):1083-94.

10. Tran TH, Lee M, Alexander S, Gibson P, Bartels U, Johnston DL, Portwine C, Silva M, Pole JD, Sung L. Lack of treatment-related mortality definitions in clinical trials of children, adolescents and young adults with lymphomas, solid tumors and brain tumors: a systematic review. BMC cancer. 2014 Dec;14(1):1-5.

11. Becker C, Graf N, Grabow D, Creutzig U, Reinhardt D, Weyer-Elberich V, Spix C, Kaatsch P. Early deaths

from childhood cancer in Germany 1980-2016. Cancer Epidemiology. 2020 Apr 1;65:101669.

12. Bhakta N, Force LM, Allemani C, Atun R, Bray F, Coleman MP, Steliarova-Foucher E, Frazier AL, Robison LL, Rodriguez-Galindo C, Fitzmaurice C. Childhood cancer burden: a review of global estimates. The Lancet oncology. 2019 Jan 1;20(1):e42-53.

13. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, Stein KD, Alteri R, Jemal A. Cancer treatment and survivorship statistics, 2016. CA: a cancer journal for clinicians. 2016 Jul;66(4):271-89.

14. Leong E, Ong SK, Jali F, Ramlee N. Childhood Cancer Survival in Brunei Darussalam. Asian Pacific Journal of Cancer Prevention: APJCP. 2020 Nov;21(11):3259.

15. González G, Garrote M, Urbaneja R, Gutiérrez M, Herráiz C, Pino V. Differences in incidence and survival to childhood cancer between rural and urban areas in Castilla y León, Spain (2003-2014): a strobe-compliant study. Medicine (Baltimore). 2018;97(41).

16. Ibrahim AS, Khaled HM, Mikhail NN, Baraka H, Kamel H. Cancer incidence in Egypt: results of the national population-based cancer registry program. Journal of cancer epidemiology. 2014 Sep 21;2014.

17. Fadhil I, Soliman R, Jaffar S, Al Madhi S, Saab R, Belgaumi A, Elhaddad A. Estimated incidence, prevalence, mortality, and registration of childhood cancer (ages 0–14 years) in the WHO Eastern Mediterranean region: an analysis of GLOBOCAN 2020 data. The Lancet Child & Adolescent Health. 2022 Jul 1;6(7):466-73.

18. Park HJ, Moon EK, Yoon JY, Oh CM, Jung KW, Park BK, Shin HY, Won YJ. Incidence and survival of childhood cancer in Korea. Cancer research and treatment: official journal of Korean Cancer Association. 2016 Jul 1;48(3):869-82.

19. de Oliveira MM, e Silva DR, Ramos FR, Curado MP. Children and adolescents cancer incidence, mortality and survival a population-based study in Midwest of Brazil. Cancer Epidemiology. 2020 Oct 1;68:101795.

20. Nanayakkara AK, Boucher HW, Fowler VG, Jezek A, Outterson K, Greenberg DE. Antibiotic resistance in the patient with cancer: Escalating challenges and paths forward. CA: a cancer journal for clinicians. 2021 Nov;71(6):488-504.

21. Gudiol C, Albasanz-Puig A, Cuervo G, Carratalà J. Understanding and managing sepsis in patients with cancer in the era of antimicrobial resistance. Frontiers in Medicine. 2021 Mar 31;8:636547.

22. Loeffen EA, Knops RR, Boerhof J, Feijen EL, Merks JH, Reedijk AM, Lieverst JA, Pieters R, Boezen HM, Kremer LC, Tissing WJ. Treatment-related mortality in children with cancer: Prevalence and risk factors. European Journal of Cancer. 2019 Nov 1;121:113-22.

23. Al-Hadad SA, Al-Jadiry MF, Ghali HH, Al-Badri SA, Al-Saeed RM, Al-Darraji AF, Sabhan AH, Fadhil SA, Hussein HM, Abed WM, Ameen NA. Treatment of childhood acute lymphoblastic leukemia in Iraq: a 17-year experience from a single center. Leukemia & Lymphoma. 2021 Dec 6;62(14):3430-9.

24. Shakibazad N, Bordbar M. Overview the Causes of Early Deaths and Advance Supportive Care in Children with Acute Lymphoblastic Leukemia: A Systematic Review. Iranian Journal of Blood and Cancer. 2022 Mar 30;14(1):1-5.

25. Noroozi M, Khalkhali HR, Bahadori R, Omidi T, Ghazizadeh F, Hejazi S, Mahdi-Akhgar M, Valizadeh R. The survival of childhood acute lymphoblastic leukemia and its related factors using competing risks model: A retrospective study from 2011 to 2019 in northwestern Iran. Middle East Journal of Cancer. 2022 Jul 1;13(3):531-42.

26. Abdelmabood S, Fouda AE, Boujettif F, Mansour A. Treatment outcomes of children with acute lymphoblastic leukemia in a middle-income developing country: high mortalities, early relapses, and poor survival. Jornal de Pediatria (Versão em Português). 2020 Jan 1;96(1):108-16.

27. Hafez HA, Soliaman RM, Bilal D, Hashem M, Shalaby LM. Early deaths in pediatric acute leukemia: a major challenge in developing countries. Journal of Pediatric Hematology/Oncology. 2019 May 1;41(4):261-6.

28. Bayoumi A. Risk Factors of Infection related mortality in Pediatric Acute Myeloid Leukemia- Single Institute Experience: 2016–2018. Journal of Pediatric Infectious Diseases Society, 2021; 2 (10), S1-S1.

29. Lins MM, Mello MJ, Ribeiro RC, De Camargo B, de Fátima Pessoa Militão de Albuquerque M, Thuler LC. Survival and risk factors for mortality in pediatric patients with acute myeloid leukemia in a single reference center

in low–middle-income country. Annals of Hematology. 2019 Jun 1;98:1403-11.

30. Morais RV, Souza MV, Silva KA, Santiago P, Lorenzoni MC, Lorea CF, Castro Junior CG, Taniguchi AN, Scherer FF, Michalowski MB, Daudt LE. Epidemiological evaluation and survival of children with acute myeloid leukemia. Jornal de Pediatria. 2021 Apr 19;97:204-10.

31. Alkhayat N, Alshahrani M, Elyamany G, Sedick Q, Ibrahim W, Hamzi H, Binhassan A, Othman M, Alshieban S, Aljabry MS, Asiri S. Clinicopathologic features and therapy outcome in childhood Hodgkin's lymphoma: a report from tertiary care center in Saudi Arabia. Journal of the Egyptian National Cancer Institute. 2021 Dec;33(1):1-9.

32. Sherief LM, Elsafy UR, Abdelkhalek ER, Kamal NM, Elbehedy R, Hassan TH, Sherbiny HS, Beshir MR, Saleh SH. Hodgkin lymphoma in childhood: clinicopathological features and therapy outcome at 2 centers from a developing country. Medicine. 2015 Apr;94(15).

33. Mansoor R, Saeed H, Wali RM, Rehman P, Abubakar M. Malnutrition, sepsis, and tumor lysis syndrome are associated with increased rate of acute mortality in mature B cell non-hodgkin lymphoma in a pediatric population-study from Tertiary Care Hospital in Pakistan. Mediterranean Journal of Hematology and Infectious Diseases. 2019;11(1).

34. Minard-Colin V, Brugières L, Reiter A, Cairo MS, Gross TG, Woessmann W, Burkhardt B, Sandlund JT, Williams D, Pillon M, Horibe K. Non-Hodgkin lymphoma in children and adolescents: progress through effective collaboration, current knowledge, and challenges ahead. Journal of Clinical Oncology. 2015 Sep 9;33(27):2963.

35. National Cancer Center. Annual report of cancer statistics in Korea in 2015. Sejong, Korea: Ministry of Health and Welfare; 2017.

36. Zhang WL, Zhang YI, Zhi T, Huang DS, Wang YZ, Hong L, et al. High-dose chemotherapy combined with autologous peripheral blood stem cell transplantation in children with advanced malignant solid tumors: a retrospective analysis of 38 cases. Oncol Lett. 2015;10(2):1047–1053.

37. Lee JA. Solid Tumors in Children and Adolescents. J Korean Med Sci. 2018 Sep 17;33(41):e269.

38. Nandan R, Sharma S, Bajpai M, Jain V, Goel P, Yadav DK. Pediatric neuroblastoma- Impact of nutritional status on complications and outcomes. Journal of Indian Association of Pediatric Surgeons. 2022 Apr 1;27(2):209
.

39. Al Tonbary Y, Badr M, Mansour A, El Safy U, Saeed S, Hassan T, Elashery R, Nofal R, Darwish A. Clinico-epidemiology of neuroblastoma in north east Egypt: a 5-year multicenter study. Oncology letters. 2015 Aug 1;10(2):1054-62.

40. Fabian ID, Abdallah E, Abdullahi SU, Abdulqader RA, Abdulrahaman AA, Abouelnaga S, Ademola-Popoola DS, Adio A, Afifi MA, Afshar AR, Aggarwal P. The Global Retinoblastoma Outcome Study: a prospective, cluster-based analysis of 4064 patients from 149 countries. The Lancet global health. 2022 Aug 1;10(8):e1128-40.