



## Childhood cancer care in the Middle East, North Africa, and West/Central Asia: A snapshot across five countries from the POEM network

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### ABSTRACT

**Background:** The Pediatric Oncology East and Mediterranean (POEM) network, through this report, provides a snapshot view of an expected child's treatment journey in five countries in the region.

**Methods:** Pediatric oncologists from cancer centers in Egypt, Lebanon, Iraq, Jordan, and Pakistan provided input on referral pathways, barriers to care, and patient outcomes, based on personal experience and published data. Outcome data were extracted from institutional registries. A literature review of articles and meeting abstracts was conducted, and results summarized.

**Results:** Countries across the Middle Eastern, North African, and West Asian region face common difficulties relating to the provision of pediatric oncology care. National registries are largely lacking, with unavailability of outcome data. Economic barriers are a common theme, leading to delays in patient diagnosis, and interruptions and abandonment of therapy. Insufficient infrastructure and human resources, high rates of toxic deaths, and lack of common national protocols are common. The establishment of successful fundraising organizations linked to specific cancer hospitals showcase several success stories, enhancing services, improving patient access, and leading to outcomes comparable to those in developed countries. All identified published literature is institution-based and from only one or a few hospitals. Therefore, outcomes at a national level likely differ due to disparate cancer care capabilities.

**Conclusion:** Well-designed national registries are essential for identifying gaps, and clear referral networks are needed to address delays to diagnosis and therapy. National and transversal programs to improve infrastructure, facilitate knowledge transfer, and promote advocacy, are needed to accelerate progress in the region.

### 1. Introduction

Treatment of childhood cancer has improved considerably over the past 30 years, with survival reaching 70–80%, and even surpassing 90% for some cancer types with appropriate therapy [1]. However, in developing countries, many patients are unable to access timely or appropriate therapy, leading to much lower survival rates and more advanced disease at presentation [2]. The Middle East, North Africa, and West/Central Asia region is a mix of high, upper-middle, and

lower-middle-income countries. In addition to the economic difficulties, the recent frequent wars in the region have destabilized the already frail infrastructure in impacted countries, and further affected the financial burden of patients and families seeking treatment for cancer. Treatment of childhood cancer, specifically, requires a well-coordinated tertiary healthcare setting for disease diagnosis and treatment planning, and in many cases, treatment is intensive, requiring substantial supportive care and skilled workforce. In low- and middle-income countries, it is estimated that a sizeable proportion of patients with childhood cancer are

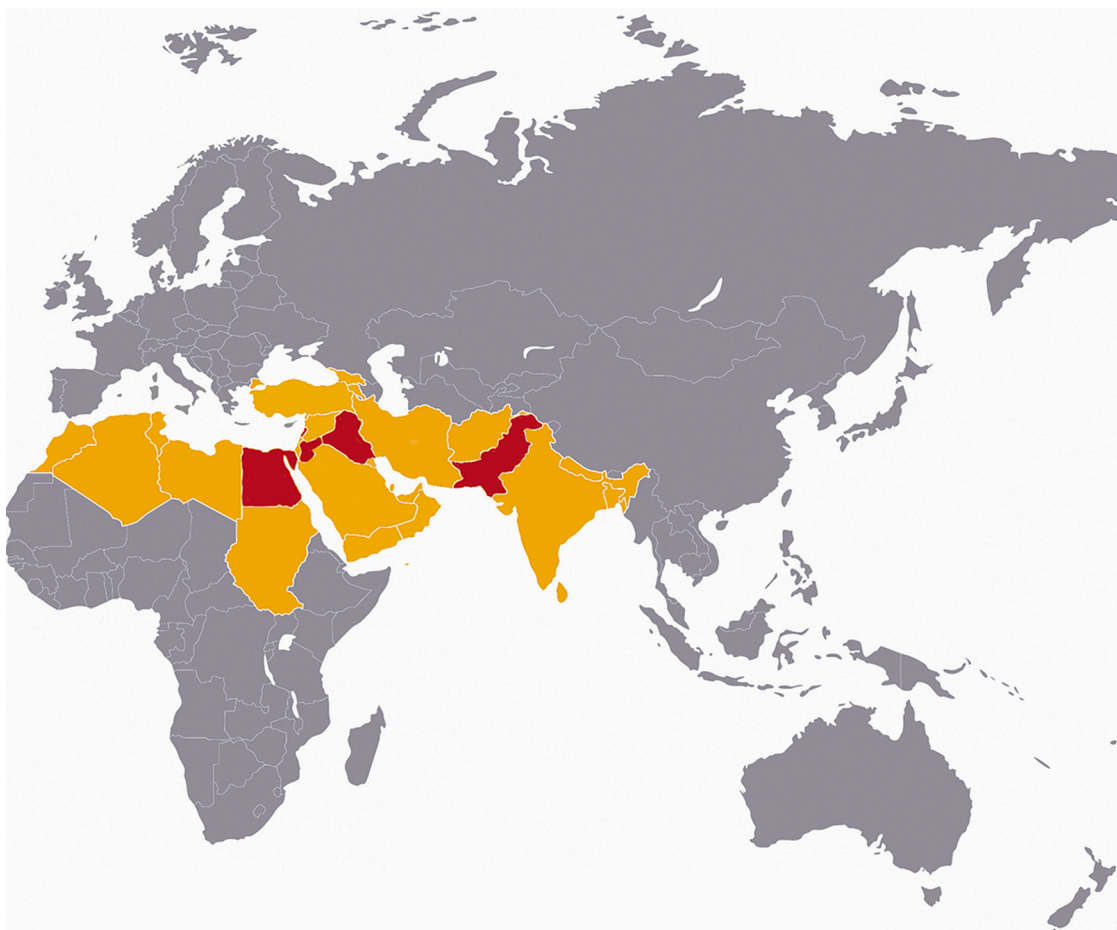
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**Fig. 1.** POEM membership includes practitioners in the following countries, shown on the map and listed alphabetically below:

Afghanistan, Algeria, Armenia, Bahrain, Bangladesh, Egypt, Georgia, India, Iran, Iraq, Jordan, Kingdom of Saudi Arabia, Kuwait, Lebanon, Libya, Morocco, Nepal, Oman, Pakistan, Palestine, Qatar, Sri Lanka, Sudan, Syria, Tunisia, Turkey, United Arab Emirates, and Yemen. The countries in red are included in this review. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

unaccounted for due to under-diagnosis, and another proportion is lost due to abandonment [3,4]. Patients who do get diagnosed have higher rates of therapy toxicity, or failure of treatment due to advanced stage at diagnosis, lack of medications and appropriate surgery and radiation therapy, and interruptions in treatment due to financial or other barriers to care [5–7].

In this report, we attempt to give a snapshot of successes and barriers in childhood cancer treatment, focusing on five countries from the Middle East, North Africa, and West/Central Asia region, where recent collaborations have been forged through the Pediatric Oncology East & Mediterranean (POEM) Group (Fig. 1). Although the strength of the healthcare systems in the region varies, as well as the availability of human and structural resources, healthcare providers in these countries share common difficulties and barriers for providing appropriate cancer care. POEM was established as a platform for collaborative activities among pediatric oncology providers, aiming to improve resources, promote knowledge, and enhance collaborative research and clinical care ([www.poemgroup.org](http://www.poemgroup.org)).

## 2. Methods

Data related to each country was collected through a common form (Supplementary File#1) filled by each of the respective authors, which included sections on A) baseline epidemiologic information and registry, and B) factors affecting decision-making in pediatric oncology referral and care including i) factors contributing to loss of patients between symptoms onset and first presentation to local healthcare facility, ii)

factors contributing to patient loss/delays after being seen in local healthcare facility and during referral to cancer clinic, iii) factors contributing to delays from presentation to cancer clinic and making a diagnosis, iv) factors contributing to loss/delays/death/outcome after diagnosis, and v) other specific points, issues, or comments. With the absence of national registries and nationwide sources of information regarding childhood cancer referral networks, infrastructure availability and pathways of clinical care, the relevant information collected is based on the experience of a tertiary referral cancer center in each of the countries, and data is estimated based on professional experience of the authors during clinical practice.

A literature search was conducted for publications relating to pediatric cancer outcomes and barriers to care relating to each of the five countries. We searched the Ovid MEDLINE database, with a date range of 2000 until January 22, 2020. Search terms included “cancer”, “tumor”, “neoplasms”, “pediatric”, “child”, “middle east”, “Iraq”, “Jordan”, “Lebanon”, “Pakistan”, “North Africa”, “Egypt”, and combination of the above terms. The resulting hits were exported to Endnote and divided in 5 groups corresponding to each country. We also conducted a review of abstracts published as part of the International Society of Pediatric Oncology (SIOP) annual conference proceedings for the years 2011–2019, to extract posters and oral presentations from each of the 5 countries. A manual review of each abstract was next done, to only include articles/abstracts focused on pediatric patients treated after the year 2000 in the 5 specific countries. Articles/abstracts focusing on specific biologic or molecular characterization, or treatment and outcome of specific rare patient subgroups within pediatric oncology,

**Table 1**  
Summary of published literature relating to barriers, treatment, and outcome of common childhood cancers in Egypt\*.

Author (Year), Hospital, City	Years included	N	Age	Tumor type	Outcome	Notes
Abdelmabood (2017), Mansoura University Children's Hospital, Mansoura	2013–2015	138	1–17 years	All cancers	Initial misdiagnosis in 84%. Median delay 37 days (patient 3 days, physician 28 days). Highest median delays: Hodgkin 240 days, Osteo 130, RMS 88, ES 72, Brain 44	Highest mean patient delay: Hodgkin 101 days. Highest referral delay: RMS 61 days, Bone 37 days
AbdelKhalek (2014), 2 hospitals, Zagazig and Bahda	2010–2012	176	0–14 years	All cancers	Initial misdiagnosis 39%. Median delay 47 days (patient 8 days, physician 28 days). Most delayed: brain tumors, lymphoma, solid tumors	Significant factors for delays: age < 5 years, low socio-economic status, low parental education
Tantawy (2014), Children's Hospital Ain Shams, Cairo	2000–2010	158	10–19 years	All cancers (blood 92%, ALL 61%)	5-year OS 45% Blood EFS 40%, solid 36%	50% of deaths due to infection
Farrag (SIOP2017), South Egypt Cancer Institute, Assiut	2006–2010	502	0–18 years	All cancers: Leukemia 49% Lymphoma 24% Solid 24%	5-year OS 45%, EFS 36%. Early deaths 21% ALL, 52% AML, 18% NHL 40% died, 19% death in induction. In 2013 improved supportive care: 29% death, 13% death in induction	85% complied with treatment
Hafez (2019), National Cancer Institute, Cairo	2011–2013	370	0–18 years	ALL 253, AML 100, Mixed phenotype 17	20% induction death. OS 51%, DFS 42%	Early death causes: infection 65%, vascular 18%
Mosaad (2017), Oncology Center, Mansoura	2011–2015	116	0–18 years	ALL	5-year OS: 86%, EFS 67%	
Tantawy (2013), 2 hospitals, Cairo & Menoufeya	2004–2005	52	1–17 years	ALL, 6% CNS-positive	7-year OS 77%, EFS 66%	Induction death 4%, remission death 4%
Shibl (SIOP2018), South Egypt Cancer Institute, Assiut	2009–2017	200		ALL, HR 47%	4-year OS 86%, EFS 82%	2% died before chemo, 2% toxic death
Rahman Sayed (2016), CCHE, Cairo	2007–2012	77	0–18 years	Lymphoblastic Lymphoma Stage IV 17%	15% died: 34% of septic shock, 31% of disease, 12% of tumor lysis syndrome	4% died before therapy, 48% in prophase or induction, 16% in consolidation or maintenance
Abdel Rahman Sayed (SIOP2019), CCHE, Cairo	2012–2018	570		Burkitt Lymphoma	5-year OS 57%, EFS 52%	27% treatment-related mortality 33% CNS-positive
Salem (SIOP2017), CCHE, Cairo	2007–2015	88		Burkitt Lymphoma	5-year OS 97%, EFS 85%	chemotherapy +/- radiation
Sherief (2015), Zagazig & Benha	2004–2012	59	3–14 years	Hodgkin, Stage IV 13%	6-year OS 95%, DFS 86%	chemotherapy +/- radiation
El-Badawy (2008), National Cancer Institute, Cairo	1999–2001	121	3–18 years	Hodgkin	5-year OS 91%, EFS 72%	chemotherapy +/- radiation
Khedr (SIOP2017), CCHE, Cairo		381		Hodgkin, Stage IV 31%	5-year OS 99–100%, EFS 94–95%	68% treated for risk pathology
Sedky (SIOP2018), CCHE Cairo	2010–2016	160		Enucleated RBL	5-year OS & EFS 55%	
Elzomor (SIOP2019), CCHE, Cairo	2010–2018	89	0–18 years	Extraocular RBL 39% Stage IV	5-year OS 98%	1% developed metastases/died
Elzomor (SIOP2019), CCHE, Cairo	2007–2017	404	0–13 years	Unilateral RBL 77% Groups D/E	OS 78%, RFS 63%	
Zamzam (SIOP2017), CCHE, Cairo	2009–2016	103	0–18 years	Localized Osteosarcoma	5-year OS 74%, RFS 73%	
Maarouf (SIOP2016), CCHE, Cairo	2008–2014	155		Localized Ewing sarcoma	3-year EFS, OS: Stage I-II: 93–100%, Stage III 82%, 94%, Stage IV 50%, 90%, Stage V 60%, 80%	Loss of heterozygosity associated with poorer outcome
Sidhom (2015), CCHE, Cairo	2007–2010	105	0–18 years	RMS, Stage IV 17%	3-year OS 67%, FFS 58%	Anaplasia worse outcome
AbdelFattah (SIOP2016), CCHE, Cairo	2007–2015	219		RMS intermediate-risk		
Fawzy (2015), National Cancer Institute, Cairo	2005–2010	100	0–18 years	Wilms, favorable histology	3-year OS 83%, EFS 64%	
El-Ayadi (SIOP2015), 2 hospitals, Cairo	2010–2013	135		Wilms 26% Stage IV		
Fadel (SIOP2016), CCHE, Cairo	2007–2015	124	0–18 years	Hepatoblastoma	7-year OS: Stages I-II 100%, Stages III-IV 31%	Ovarian tumors
Ali (2018), South Egypt Cancer Institute, Assiut	2005–2015	40	0–18 years	Malignant germ cell tumors, 7% Stage 4	Extragenital Stage III & IV: 5-year OS 78% & 63%; EFS 74% & 68%. Ovarian Stage III & IV: OS 100% & 33%	
Arafah (SIOP2017), CCHE, Cairo	2007–2016	75		High risk extra-cranial germ cell tumors	5-year OS 100% (LR), 96% (IR), EFS 88% (LR), 91% (IR)	
Ahmed (SIOP2017), CCHE, Cairo	2007–2016	47		Extra-cranial germ cell tumors	3-year OS 94%, EFS 91%	
Elzomor (2018), 2 hospitals, Cairo	2011–2014	136	0–18 years	IR NBL	3-year OS 40%, EFS 23%	SCT: 3 year OS 66%, vs 24% for those who did not
Ibrahiem (SIOP2019), National Cancer Institute, Cairo	2008–2015	133		HR NBL	2-year OS 34%, PFS 29%	37% SCT, 24% early progression
AlSheikh (SIOP2015), Alexandria	2010–2014	54		HR NBL	5-year OS 55%, PFS 75%	
	2008–2013	53	0–18 years	Medulloblastoma, HR 85%		

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Table 1 (continued)

Author (Year), Hospital, City	Years included	N	Age	Tumor type	Outcome	Notes
<i>Mustafa (SIOP2017), CCHE, Cairo</i>						
<i>Hammad (SIOP2019), National Cancer Institute, Cairo</i>	2009–2014	47		Ependymoma Grade II: 68%	3-year OS 44%, PFS 43%	10% died early before assessment

\*SIOP abstracts in italics, published articles in regular font.

N: number of patients, Osteo: osteosarcoma, RMS: rhabdomyosarcoma, ES: Ewing sarcoma, ALL: acute lymphoblastic leukemia, OS: overall survival, EFS: event-free survival, AML: acute myeloid leukemia, NHL: non-Hodgkin lymphoma, DFS: disease-free survival, CNS: central nervous system, HR: high-risk, RBL: retinoblastoma, RFS: relapse-free survival, FFS: failure-free survival, LR: low risk, IR: intermediate risk, NBL: neuroblastoma, SCT: stem cell transplant, PFS: progression-free survival.

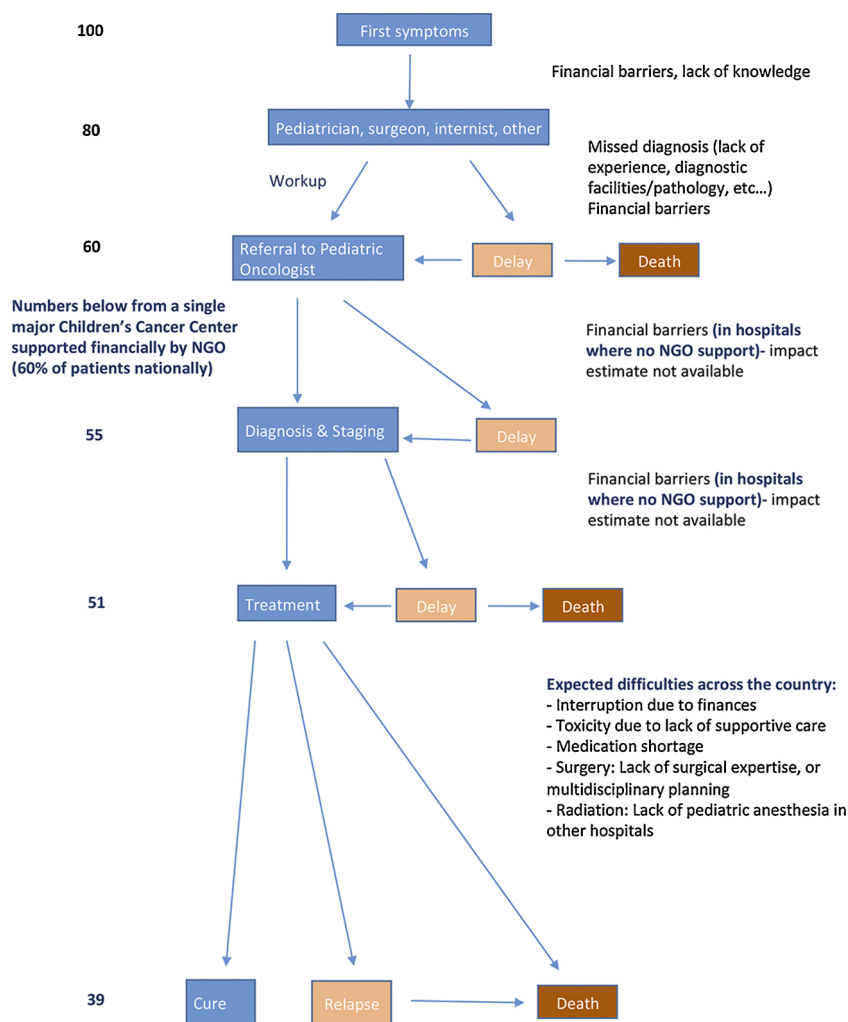


Fig. 2. Pathway of childhood cancer care in Egypt: patient number estimates based on professional personal experience, single institution registry data, and publications.

were excluded. The remaining articles were tabulated, with manual extraction of relevant information relating to patient treatment, outcome, and barriers to care, and presented in the accompanying Tables. For redundant abstracts or articles, we used the more inclusive and recent publication.

### 3. Results

#### 3.1. Egypt

With the absence of a national cancer registry, the incidence rate of childhood cancer in Egypt is difficult to estimate. The population-based

registry at the Gharbiyah province, an area with a population of around 4 million, has been active since 1999 [8], but specific pediatric cancer data has not been published. The Children’s Cancer Hospital in Egypt (CCHE) is the largest pediatric cancer hospital in the country, annually enrolling approximately 3000 patients younger than 18 years, an estimated 50% of childhood cancer cases in a country with a population of around 100,000,000. While the outcome of patients with childhood cancer is not available at a national level, a review of the published literature and meeting abstracts that report patient outcomes and barriers to care in Egypt is presented in Table 1. At the CCHE, and based on the prospective institutional registry data, the estimated 5-year overall survival for children newly diagnosed in the years 2007–2018 with

**Table 2**

Summary of published literature relating to barriers, treatment, and outcome of common childhood cancers in Lebanon.

Author (Year), Hospital, City	Years included	N	Age	Tumor type	Outcome	Notes
Muwakkat (2012), CCI, Beirut	2002–2009	111	1–21 years	ALL: Intermediate risk: 41%	1% induction death; 4% died in remission, 5-year OS 88%, EFS 78%	Significant toxicity but improved cure rates.
Farah (2015), St George Hospital, Rizk Hospital, Beirut	2002–2010	24	1–24 years	AML (25% APL)	Early death 17%. 50% APL death. 50% remission after cycle 1. DFS 30%	Survival: 50% of patients < 10 years; 0% of those > 10 years
Al-Haddad (2019) CCI, Beirut	2012–2017	40	0–5 years	Retino-blastoma	33% ocular salvage, 2-year OS 98%	66% Group D/E
Abou Ali (2014) CCI, Beirut	1999–2012	39	0–18 years	Ewing sarcoma 21% metastatic	5-year OS & EFS: 76% & 58% (localized), 40% & 38%, (metastatic)	Financial barriers overcome by organization support
Abou Ali (2019), CCI, Beirut	2001–2012	38	1–18 years	Osteosarcoma 24% Stage IV	Localized: 5-year OS 81%, EFS 68%. Metastatic: 5-year OS, EFS 42%	66% had delay in local control by more than 4 weeks
Saab (2016), multiple hospitals	2012–2015	35	1–18 years	Bone Tumors, Centralized funded surgeries	5% toxic death, 5% lost to follow-up. Surgery delay 10%	Change in diagnosis in 10% (central pathology review)
Salman (2012), CCI, Beirut	2002–2012	23	0–17 years	RMS Group III: 65% Group IV: 4%	5-year OS 83% 5-year DFS 64%	Higher rate of local relapse
Rabeh (2016), CCI, Beirut	2002–2013	35	0–16 years	Wilms Tumor, Stage IV: 26%	3-year OS 88%, EFS 86%	1 toxic death

N: number of patients, ALL: acute lymphoblastic leukemia, OS: overall survival, EFS: event-free survival, AML: acute myeloid leukemia, APL: acute promyelocytic leukemia, DFS: disease-free survival, RMS: rhabdomyosarcoma, DFS: disease-free survival.

acute lymphoblastic leukemia stands at 80%, Hodgkin lymphoma 96%, Burkitt lymphoma 81%, acute myeloid leukemia 54%, and retinoblastoma 92%, with an overall survival across all patient groups approximating 71%. To note, and as true for other countries discussed below, this data is from a well-equipped tertiary care multidisciplinary cancer center supported by a non-governmental fundraising institution to alleviate financial barriers to care. Thus, it reflects the best-case scenario in the country setting, and results likely cannot be extrapolated to reflect patients treated elsewhere in the country. While the CCHE is a free-standing pediatric cancer center, other hospitals typically admit patients to either a pediatric oncology ward within a general hospital, or a general pediatric ward, depending on hospital size.

Fig. 2 describes the expected pathway of a child with cancer in Egypt, from the first presentation until the end of treatment, with estimated rates of patient loss along the way. As can be seen from Table 1, while excellent outcomes are achievable in centers with the needed infrastructure and financial support, common barriers to care still include delays in diagnosis within the healthcare networks, deaths due to infectious causes and toxicity, and advanced stage at presentation. At the CCHE, referred patients are assessed for eligibility, and a waiting list process is followed. Approximately 7% of patients are referred to other governmental hospitals due to beds unavailability and critical condition precluding waiting time.

Two studies in Egypt examined delayed diagnosis in childhood cancer. Delays seem to be associated with patient age < 5 years, low socioeconomic status, and low level of parental education [9]. A median delay of 37 and 47 days was noted respectively in the two studies, primarily attributed to delays after presentation to a healthcare provider. An initial erroneous diagnosis was noted in 39% and 74% in the two studies, more frequently in patients with brain and solid tumors [9,10]. In one study, the briefest delays were associated with germ cell tumors and leukemia, and the longest delays were in children with brain tumors [9]. In the second study, most significant delays were for Hodgkin lymphoma (median of 240 days), sarcomas (median 70–130 days), and brain tumors (median 44 days) [10]. In our experience, other common factors associated with delays include lack of healthcare coverage and transportation cost, affecting 15–20% of patients [author's estimate, AAH]. Of note, there have been several satellite oncology centers established over the past few years, and awareness campaigns conducted. NGOs have helped cover costs of diagnosis and treatment. However, considerable difference in infrastructure and workflow exist, and delays relating to financial coverage, procurement of medications by the family, availability of beds, toxicity and infectious complications, all still occur and contribute to a worse outcome [11]. In addition, due to unstable political conditions in regional countries such as Yemen, Libya,

and Syria, patients from those countries are increasingly presenting for diagnosis and treatment, yet there are no accurate data regarding numbers, financial coverage, and delays in accessing care.

### 3.2. Lebanon

Lebanon is a small country with a population of approximately 4.5 million nationals and a recent population expansion by approximately 1.5 million refugees displaced from neighboring Syria due to war. Lebanon has suffered from sequential wars, economic instability, and political unrest since it gained its independence in 1943. Despite those continuous challenges, Lebanese private institutions and NGO initiatives have continued to help advance medicine and sciences in Lebanon, including an improvement in cancer care and outcome, although major challenges still exist. Lebanon has had a national cancer registry since 2005; however, the quality of data collected is suboptimal, and the registry has been frequently interrupted over the years. In addition, it captures all patients diagnosed in Lebanon, including those seeking consultation from neighboring Syria and Iraq, inflating the number of registered cancer cases relative to the Lebanese population. The most recent numbers reported by the registry document around 360 cases per year of childhood cancer up to 18 years of age [12].

Pediatric patients with cancer are treated at multiple hospitals across Lebanon, with a concentration of most hospitals within the capital Beirut, and a paucity of hospitals in South Lebanon and the Beqaa area. A major advancement in childhood cancer care in Lebanon was the establishment of the Children's Cancer Institute (CCI) in 2002, supported by the Children's Cancer Center of Lebanon (CCCL) Foundation, a fundraising NGO, to cover direct treatment costs. This has significantly improved access to care irrespective of financial means. While the CCI is an exclusive childhood cancer center set within a larger multi-specialty hospital complex, children treated for cancer elsewhere in the country are admitted to a pediatric oncology ward or to a general pediatric ward within a general hospital.

The CCI institutional pediatric cancer registry prospectively collects diagnosis and outcome data. With an annual acceptance of 95–100 newly diagnosed patients, CCI treats approximately 35–40% of childhood cancer cases in the country. Through programmatic initiatives, collaborations with pediatric oncologists across the country have enabled access of patients to specialized diagnostics, surgical procedures, and pediatric radiation oncology [13,14].

The institutional registry shows an estimated 5-year overall survival for children newly diagnosed in the years 2002–2019 with acute lymphoblastic leukemia of 88%, Hodgkin lymphoma 98%, Burkitt lymphoma 75%, acute myeloid leukemia 60%, and retinoblastoma 95%.

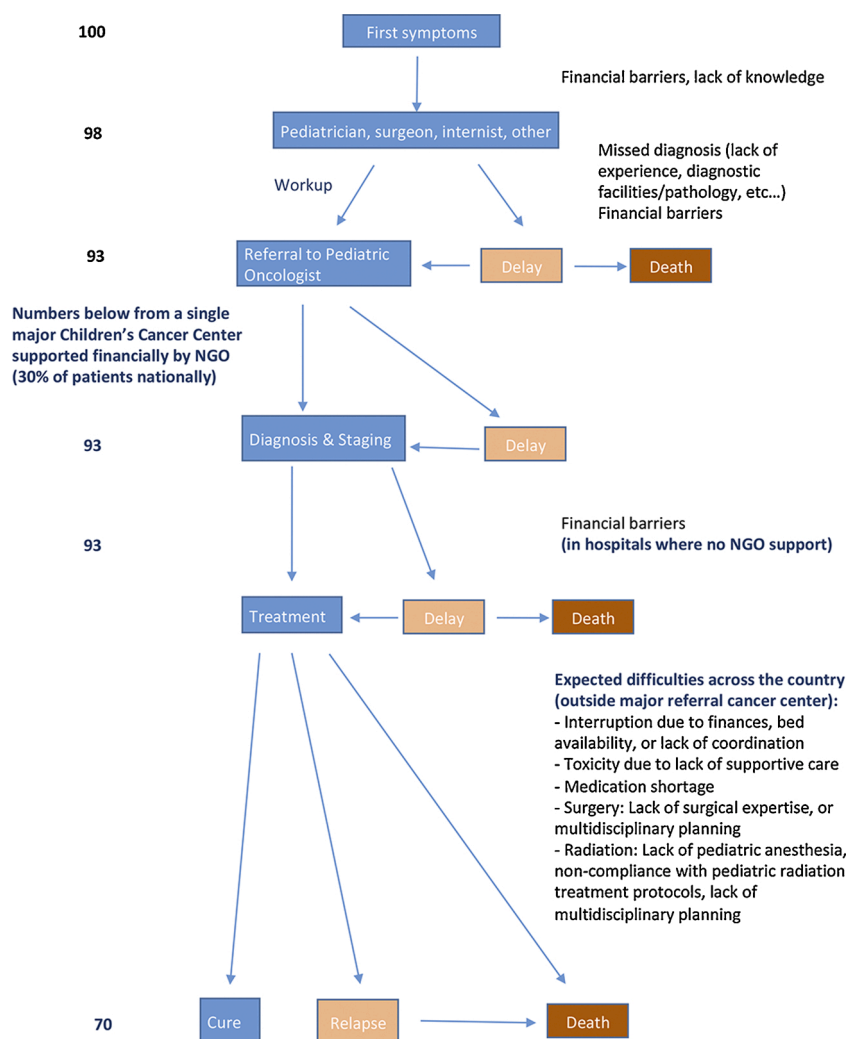


Fig. 3. Pathway of childhood cancer care in Lebanon: patient number estimates based on professional personal experience, single institution registry data, and publications.

At the CCI, patients receive treatment in a multidisciplinary cancer center, with closely coordinated care, availability of subspecialty services, support by social work and child life services, and alleviation of financial burden by the CCCL. We reviewed the published literature to extract all publications that report patient outcomes and barriers to care in Lebanon (Table 2). Of note, all but one are from a single cancer center with excellent NGO support, and therefore difficult to extrapolate as national outcomes. Over the past 15 years, there have been several NGOs raising funds and awareness for the treatment of childhood cancer. The exact impact, however, is difficult to measure. Delays due to financial barriers are still relatively common. Fig. 3 describes the expected pathway of a child with cancer in Lebanon, from the first presentation until the end of treatment, with estimated rates of patient loss.

### 3.3. Iraq

The UN described the Iraqi healthcare system before 1980 as one of the best in the Middle East [15]. After 4 wars, 13-year sanctions, and continuous sectarian violence, Iraq has had major disruptions and dissolution of institutions and human resources. Healthcare services suffer from overcrowding, limitations in diagnostic facilities, and lack of modern modalities. Substantial gaps in knowledge, ineffective referral systems, lack of national protocol guidelines, and inadequate numbers of pediatric oncologists, all contribute to suboptimal care for children with cancer.

While there is a paucity of publicly available national statistics, based on a population of 38 million, and assuming incident rates similar to developed countries, approximately 1200–1500 cases of childhood cancer (age 0–14 years) is estimated annually across Iraq. Table 3 summarizes a review of the published literature and meeting abstracts that report patient outcomes and barriers to care, highlighting high rates of early deaths, patient abandonment, and toxic complications. The Children's Welfare Teaching Hospital (CWTH) within the Medical City Complex in Baghdad, is a governmental tertiary care center that accepts an average of 300 new pediatric cancer cases annually (range 250–400 per year). At CWTH, as in many other hospitals across the country, children with cancer are admitted to a pediatric oncology ward, situated within a general hospital. In smaller hospitals, children may be treated on general pediatric wards.

Major barriers to patient access include displacement, financial distress, security issues, and lack of confidence in the healthcare system, with many families seeking traditional/alternative medicine [author's experience]. In 2012, a study interviewing 346 newly diagnosed patients uncovered a diagnosis delay of 55 days (range 3–1093 days), with a median delay of time to first presentation of 4 days (range 1–365 days), and a median delay after seeing a physician of 43 days (range 1–1079 days) [unpublished data, MAJ]. The median number of doctor visits was 5 (range 1–29), with 56% of children seen by more than 3 physicians before being referred to CWTH. The impression was a benign condition in 70%, with the most common misdiagnosis (60%) being infection.

**Table 3**  
Summary of published literature relating to barriers, treatment, and outcome of common childhood cancers in Iraq\*.

Author (Year), Hospital, City	Years included	N	Age	Tumor type	Outcome	Notes
Al-Hadad, (2011) CWITH Baghdad	2000–2009	1227	0–14 years	All cancers, excluding brain tumors	<b>ALL:</b> 2000–2002, 239 patients, 5-year EFS 47%, abandoned 23% 2003–2005, 265 patients, 3-year EFS 40–57%, abandoned 30% 2006, 99 patients, 3-year EFS 65%, abandoned 24% <b>APL:</b> 2003–2009, 48 patients, 4-year EFS 43% <b>AML:</b> 2000–2007, 107 patients, EFS 5–7% <b>NHL:</b> 2000–2005, 239 patients, OS 66%, EFS 53% <b>HL:</b> 2005–2009, 67 patients, EFS 70%, abandoned 5% <b>WT:</b> 2005–2009, 90 patients, OS 51% <b>RBL:</b> 1999–2006, 32 patients, DFS 23%, death 27%, abandoned 23% <b>Bone tumors:</b> 1999–2009, 41 patients, OS 56%, abandoned 19%	Wars, sanctions, political instability, poverty, malnutrition, transportation issues. International collaboration had major impact: Provision of drugs and medical supplies, scientific workshops, telemedicine programs. Led to 1) a decrease in induction mortality in ALL from 24% to 10% after introduction of pre-phase steroids and 2) in APL from 95% to 5% after introduction of retinoic acid. 3) Changing diagnosis of 20% of pathology samples
Al-Jadiry, (2013) CWITH Baghdad	2007–2008	256	0–15 years	All cancers	<b>HL:</b> 2005–2009, 67 patients, EFS 70%, abandoned 5% <b>WT:</b> 2005–2009, 90 patients, OS 51% <b>RBL:</b> 1999–2006, 32 patients, DFS 23%, death 27%, abandoned 23% <b>Bone tumors:</b> 1999–2009, 41 patients, OS 56%, abandoned 19%	High incidence of hepatitis B with leukemia; 34% in those receiving more than 3 units of blood
Al-Kzayer, (2012), 5 hospitals	2009–2011	264	0–15 years	ALL	Remission: 86% Induction death 9%.	International collaboration helps diagnosis
Al-Haddad, (SIOP2019) CWITH Baghdad	2000–2016	1415	1–15 years	ALL	2-year OS 75%, EFS 60%.	Multiple treatment protocols. Improvement in recent era
Al-Jadiry, (SIOP2019) CWITH Baghdad	2003–2011	59	0–1 year	Infant ALL	Remission 51%, induction death 40%. 2-year OS 30%, EFS 21%.	Improvement in recent era
Moleti, (2011) CWITH Baghdad	2000–2011	239	0–15 years	NHL: 16% Stage IV	Death in 29%, abandoned 12%, 2-year OS 66%, EFS 53%. Infectious and metabolic toxicities	Reduced doses due to lack of facilities and supportive care
Othman, (SIOP 2018) Kurdistan	2009–2016	38	3–18 years	HL, 61% stage III/IV	OS 88%, EFS 85%	
Majeed (2019), Kurdistan	2009–2015	31	0–18 years	Ewing sarcoma	5-year OS 19%	61% localized
Star, (SIOP 2018) Sulaimaniyah	2009–2015	31	1–18 years	Ewing sarcoma	5-year OS 19%; RFS 34%	Lack of multi-disciplinary team and lack of adequate oncology facilities
Al-Jadiry, (SIOP2018) CWITH Baghdad	2004–2013	198	2–12 years	Wilms Stage IV 20%	5-year OS 35% (71 patients, 2004–2008) to 64% (127 patients, 2009–2013), Death 18%; Abandoned 28%.	Delayed referral of 15 patients post nephrectomy. Recent period better outcome
Ali, (SIOP2018) North Iraq	2007–2017	50	0–10 years	Wilms Stage IV 6%	4-year OS 80%, EFS 60%	

\* SIOP abstracts in *italics*, published articles in regular font.

N: number of patients, ALL: acute lymphoblastic leukemia, EFS: event-free survival, APL: acute promyelocytic leukemia, AML: acute myeloid leukemia, NHL: non-Hodgkin lymphoma, OS: overall survival, HL: Hodgkin lymphoma, WT: Wilms tumor, RBL: retinoblastoma, DFS: disease-free survival, RFS: relapse-free survival.

After presenting to CWTH, nearly 13% of inpatients died within 30 days of the first admission, 58% of whom had leukemia.

Lack of reliable diagnostics, including pathology services, leads to frequent diagnostic errors and dilemmas, and the high cost of essential diagnostic modalities not offered at governmental hospitals (such as MRI, CT/PET, immunostaining, flow cytometry, FISH, genetic studies) poses significant financial barriers. Refusal to undergo surgery is frequently encountered, particularly for patients with bone tumors and retinoblastoma [author's experience]. Once treatment is initiated, the long queue at the governmental hospitals, in addition to limitations in therapeutic tools, leads families to shift care to private hospitals, at significant financial burdens. In a survey conducted in 2017, Iraq was among the countries with severe lack of routine access to essential pediatric cancer medication [16]. Despite all these barriers, some improvements implemented over the past few years are listed in Table 4.

At CWTH, the institutional registry computed 5-year overall survival for children with acute lymphoblastic leukemia has increased from 20% for patients diagnosed in 1994 to 54% for patients diagnosed in 2002, at which time the abandonment rate was approximately 25%. In the most

recent era (2000–2016), 5-year event-free survival is at 45%, with the abandonment of 16%, and induction mortality declining from 21% to 9% after introducing pre-phase steroids [17–19]. For Hodgkin lymphoma, 3-year event-free survival rates are at 82%, while for non-Hodgkin lymphoma are at 56% with an 11% early death rate [20, 21]. Patients with AML have a 2-year EFS of 34%, and APL 54–65%, with a 13–19% induction mortality. Notably, the majority (approximately two-thirds) of patients with solid tumors present with advanced-stage disease [unpublished data, MAJ]. Fig. 4 describes the expected pathway of a child with cancer in Iraq from the first presentation until the end of treatment, with estimated rates of patient loss along the way.

#### 3.4. Jordan

Jordan has an established national cancer registry; however, it does not provide data on patient outcomes and it reports pediatric patients up to the age of only 15 years. A milestone in childhood cancer care in Jordan was the establishment of the King Hussein Cancer Foundation

**Table 4**  
Recent projects leading to improved childhood cancer care capacity in CWTH, Iraq.

Service	Change	Impact	References
Essential Medications	Prior to 2003, <10% of the list was available. After 2009 increased to 70%. Declined again with ISIS war in 2014		[15,19]
Telemedicine	e-Learning program in 2003 by INTERSOS between CWTH and Sapienza University in Rome	Satellite telemedicine service, training and consultation, significant impact on management of leukemia & lymphoma	
Retinoic Acid procurement	Introduction of retinoic acid and adapted APL protocol	Decrease induction mortality and improved survival	[45,46]
Treatment guidelines	Introduction of pre-phase steroid for ALL in 2008	Decrease induction mortality rate of ALL by 10%	[17,18, 47]
Pathology consultation	Collaboration with Sapienza University in Rome	Mailing of paraffin-embedded tissue blocks in addition to periodic lectures. Currently a 10-year collaboration with an overall review of more than 1000 pathology specimens, achieving a change in the diagnosis of 20% of cases in the first 5 years, 10% in the last five years, and scientific publications	[48–55]
Japan Iraq Medical Network (JIM-NET)	Started in 2004, medical supplies to 5 hospitals, medical examinations in refugee camps.	Collaborative work has enhanced research culture and resulted in publications in leukemia genetics	[56–60]
JICA, JIMNET	Nursing training	Improved nursing practices	
Improvement in diagnostic tools	Acquisition of MRI and CT scans in 2010, Flow Cytometry in 2013, PET scan in 2018, immunostaining in 2019	Improvement in access to diagnostic tests and staging	

ALL: acute lymphoblastic leukemia, APL: acute promyelocytic leukemia, MRI: magnetic resonance imaging, CT: computed tomography, PET: positron emission tomography.

and Center (KHCC) in 2002. This multidisciplinary cancer center allows accessibility to coordinated state-of-the-art treatment, with the availability of the needed subspecialties and treatment modalities. KHCC treats an average of 450 new cases younger than 18 years of age annually, accounting for approximately 70% of pediatric cancer cases in the country and a varying number of non-Jordanians. While KHCC is a free-standing cancer hospital with a dedicated pediatric cancer unit, most other hospitals in the country treat children with cancer on pediatric oncology wards within a general hospital, or on general pediatric wards.

Survival rates of Jordanian children with ALL was reported in the CONCORD-2 and CONCORD-3 population registry-based studies [22, 23]. In the CONCORD-2 study, low survival estimates (15–16%) and the high rates of loss-to-follow up (77%) are inconsistent with other literature from Jordan that reflect the same era [24], likely impacted by poor data recovery. In the following CONCORD-3 study [23], the lost-to-follow-up rate of reporting was much lower at 5%, and the 5-year

survival rates for children with childhood (0–14 years) ALL was 75%, 89%, and 88% for children diagnosed during the years 2000–2004, 2005–2009, and 2010–2014, respectively. For childhood lymphoma, numbers were 92%, 91%, and 87%, respectively, while for brain tumors they were 73%, 66%, and 57%. The authors caution though that linkage of registry data with the national death index in Jordan was insufficient in this study, because only about 70% of deaths are certified, so the actual survival numbers may be lower than reported.

The institutional registry at the KHCC allows for prospective patient follow-up, and its data show an estimated 5-year overall survival for children diagnosed in the years 2006–2017 with acute lymphoblastic leukemia of 89%, Hodgkin lymphoma 96%, Burkitt lymphoma 89%, acute myeloid leukemia 52%, and retinoblastoma 95%. As for other cancer centers detailed in this report, these rates are likely not reflective of the remainder of the country, as availability of needed support may not be readily available in smaller, peripheral hospitals.

Table 5 summarizes a review of the published literature and meeting abstracts that report patient oncology outcomes and barriers to care in Jordan. While nationals have universal healthcare coverage, non-nationals – especially patients seeking care from neighboring Iraq and Syria - frequently experience delays in diagnosis due to funding barriers. Thus, there can be prolonged delays of 1–6 months for such patients until they are directed to KHCC, after which process is similar to that for Jordanian patients. In addition, based on the authors' experience, patients with brain tumors and bone cancers frequently present after significant delays. During treatment, transportation and accommodations can be a major challenge to the continuity of care; the continuous support of the foundation is needed to alleviate these obstacles. Fig. 5 describes the expected pathway of a child with cancer in Jordan.

### 3.5. Pakistan

With a population of approximately 200 million and with 40% in the pediatric age group, 8–12,000 children are estimated to develop cancer in Pakistan annually. However, the only population-based report is from the district of Lahore [25], showing an age-standardized incidence rate for 0–19 year old of 15.4 per 100,000 individuals. In the Punjab province, a population-based registry has been active for a few years and will be a useful source of data [25]. A city wide registry has also been formed in Karachi; however, participation is voluntary. Notably, only about 5000 new patients can be accounted for at the various childhood cancer treating facilities in the country, suggesting that a large proportion remain undiagnosed. This figure also included many patients from Afghanistan who travel to Pakistan for their care; the exact numerical contribution of these patients is not known. Outcome data is not available at either hospital or population levels, but publications are starting to document outcomes and can provide some insight into numbers and barriers to care (Table 6), highlighting high rates of delayed diagnosis, malnutrition, abandonment and toxic deaths.

The Aga Khan University (AKU) Hospital in Karachi annually treats about 200 new cases of cancer in patients younger than 18 years of age, approximately 4% of diagnosed childhood cancer cases across Pakistan. At Aga Khan University Hospital, as with most other hospitals in Pakistan, children with cancer are treated in dedicated pediatric oncology ward and outpatient unit, within a general hospital complex. While an institutional cancer registry exists, no outcome data are available. Publications and estimates report the 5-year overall survival for ALL to range between 45–63% [26,27]; whereas overall survival for Hodgkin Lymphoma ranges 89–94% [28,29]; and for non-Hodgkin Lymphoma 55–68% [30,31]. A recent informal assessment for retinoblastoma for patients diagnosed in the past 10 years across Pakistan estimated 5-year survival at 45%, with a high rate of advanced stage (25–35%) and abandonment that reaches 30% especially when enucleation is recommended [author estimate, AB]. Most hospitals do not provide curative intent therapy for AML or select only 'good risk' patients for treatment.

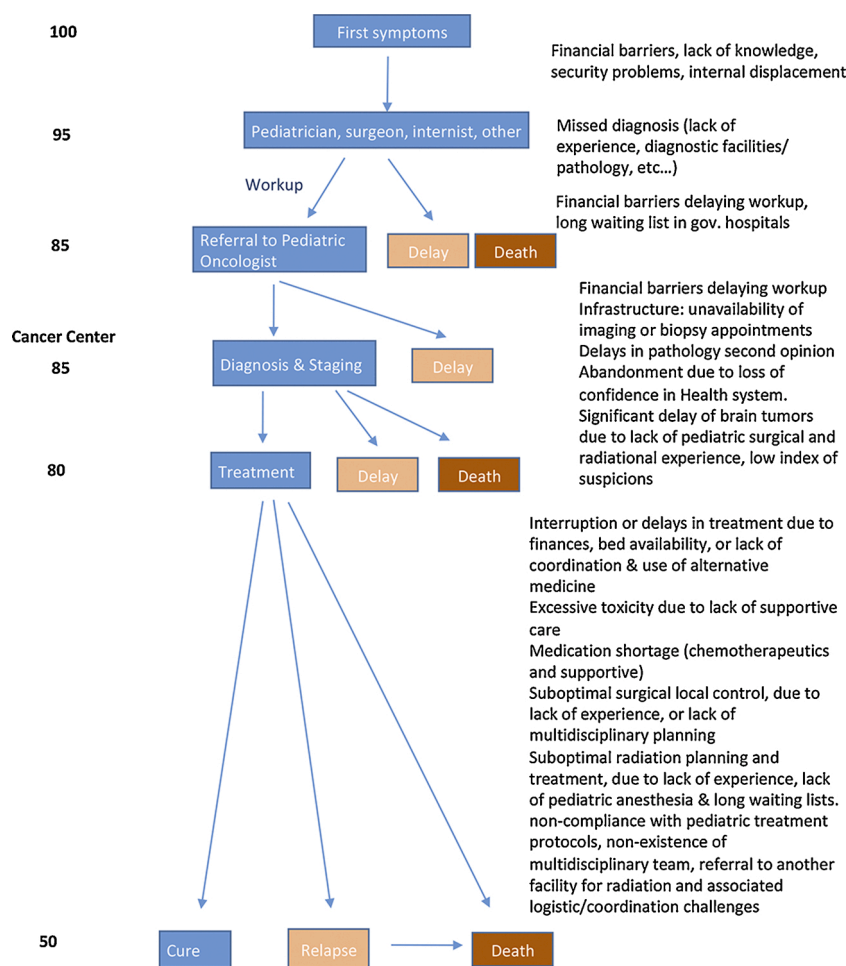


Fig. 4. Pathway of childhood cancer care in Iraq: patient number estimates based on professional personal experience, single institution registry data, and publications.

Barriers to childhood cancer care in Pakistan include financial means, where despite the establishment of governmental and non-governmental organizations providing subsidized or free medical care, the indirect cost of treatment, such as loss of income, has a major impact. There are no standard referral networks, with the process depending largely on health care provider and family preference. Delayed presentation results in a high proportion of patients with advanced disease, translating into poor outcomes. A significant proportion of patients with Hodgkin Lymphoma present with a history of empirical anti-tuberculous treatment for lymphadenopathy, contributing to delays. The Pakistan Society of Pediatric Oncology has been working to increase pediatric cancer awareness within the medical community, and there seems to be an increase in the referral to the cancer centers over the past few years, with overstretching of the existing capacity, although no documented numbers are available.

A study in 2016 reported a median time to diagnosis of 6.5 weeks, ranging 1–78 weeks [26]. One center reported a mean duration of 11.8 months between initial symptoms and first consultation for patients with retinoblastoma [32]. Abandonment rates are highest for patients with brain tumors (46%) and solid tumors (31%) [33]. Toxicity of chemotherapy, including infections, is a major contributor to patient mortality [26,27,34]. Notably, up to 50% of children presenting with cancer are malnourished [26,35]; however, there is no data on its direct contribution to toxicity, delays, or treatment failure.

On average, one pediatric oncologist sees more than 100 patients per year in Pakistan. The recent subspecialty certification approval by the College of Physicians and Surgeons of Pakistan has resulted in a much-

needed increase in locally trained and certified pediatric oncologists since 2018. The Pakistan Society of Pediatric Oncology has supported the development of a pediatric oncology nursing group, conducting workshops and providing training opportunities. Disease-specific working groups have been established, leading to collaborative national guidelines for retinoblastoma, and multidisciplinary neuro-oncology tumor boards. National protocols for ALL and HL are under development, for the unification of treatment planning across the country. The number of cancer centers has increased as well, with a subsequent improvement in the experience of radiologists and pathologists in pediatric oncology care. The government or charities financially support most children’s cancer centers; however, the cost of hospital equipment remains high, posing a barrier for acquisition and use. Fig. 6 describes the expected pathway of a child with cancer in Pakistan.

#### 4. Common barriers and the way forward

This report describes some of the common and specific challenges, barriers to care, and successes in childhood cancer treatment across five countries within the POEM network. Table 7 summarizes the most common noted barriers across all 5 countries, with the extent of impact based on the literature review and authors’ experiences.

Probably the most common challenges across the diagnosis and treatment spectrum are financial barriers to care. In Egypt, Lebanon, and Jordan, the successful establishment of fundraising non-governmental foundations linked to multidisciplinary cancer centers, has enabled

**Table 5**

Summary of published literature relating to barriers, treatment, and outcome of common childhood cancers in Jordan\*.

Author (Year), Hospital, City	Years included	N	Age	Tumor type	Outcome	Notes
Halalshah (2011) KHCC, Amman	2003–2009	300	1–18 years	ALL, Standard-risk: 39%, High-risk: 8%	Induction death 1% Remission death: 2% 5-year EFS 80%, OS 89%	
Madanat (2016) KHCC, Amman	2003–2014	63	0–18 years	T-cell ALL	5-year OS 77%, EF 80%	(20% Early T-cell Precursor)
Deebajah (SIOP2015) KHCC, Amman	2006–2015	173	3–18 years	HL Stage IV: 17%	5-year EFS 92%, OS 99%	50% bulky disease
Yousef (2018), KHCC, Amman	2012–2016	50	0–5 years	RBL 90 eyes, d-E: 63%	Eye salvage rate 66%	
Halalshah (SIOP2019) KHCC, Amman	2009–2017	79	0–18 years	Osteosarcoma	5-year EFS 50%, OS 63%	Lung metastases 19%; Multiple sites 8%
Ismael (SIOP 2019) KHCC, Amman	2003–2018	665	0–18 years	Sarcoma	17% had pathology changed after referral	
Al-Jumaily (2013) KHCC, Amman	2004–2008	45	0–18 years	RMS Stage III: 49% Stage IV: 15%	4-year PFS: 61%, OS 72%	
Sultan, I (SIOP2013), KHCC, Amman	2006–2012	60	0–18 years	WT Stage IV: 20%	2-year survival similar to North American SEER results	
Halalshah (SIOP2015), KHCC, Amman	2006–2014	61	0–11 years	NBL Stage IV: 87%	5-year EFS 27%, OS 34% SCT: 42 patients	N-MYC amplification: 45% (23/51 tested)
Amayiri (SIOP2018), KHCC, Amman	2003–2015	81	2–18 years	Medulloblastoma High risk 53%	5-year EFS 70%, OS 69% (M0 81%; M1-M3 44%)	Median time to radiotherapy: 45 days (17–155 days)
Amayiri (SIOP2015), KHCC, Amman	2007–2013	349	0–18 years	CNS tumors LGG 30%, MBL 24%, HGG 20%	5-year-OS: LGG 94%, MBL 60%, Ependymoma 53%, 3-year OS for HGG 14%	Surgery in 85% Chemotherapy +/- radiation 50%
Al-Jumaily (SIOP2011), KHCC, Amman	2004–2009	65	0–18 years	LGG 66% pilocytic astrocytoma	3-year PFS: surgery 75% multimodal 44%	

\* SIOP abstracts in *italics*, published articles in regular font.

N: number of patients, ALL: acute lymphoblastic leukemia, EFS: event-free survival, OS: overall survival, HL: Hodgkin lymphoma, RBL: retinoblastoma, RMS: rhabdomyosarcoma, PFS: progression-free survival, WT: Wilms tumor, NBL: neuroblastoma, SCT: stem-cell transplant, CNS: central nervous system, LGG: low grade glioma, MBL: medulloblastoma, HGG: high grade glioma, PFS: progression-free survival.

coverage of direct treatment costs, recruitment and training of subspecialists and multidisciplinary teams, and successful cancer centers in the region, reporting patient outcomes comparable to those in developed countries. However, their scope still does not suffice to ensure treatment for every child with cancer in these countries, indicating the need for more global and national strategies for affordable healthcare delivery in pediatric cancer treatment.

In addition, the influx of displaced patients and refugees with no healthcare coverage for cancer treatment to many countries in the region - specifically Lebanon, Jordan, Egypt, and Pakistan, has further increased the stress on the respective healthcare systems and NGOs. This has amplified the barriers to care for this increasing patient population, where most outcomes remain undocumented [36–40].

National pediatric cancer healthcare plans, along with fundraising non-governmental organizations, could form a model to extend access to reach every child with cancer in the country. Most importantly, the establishment of clear referral networks through governmental healthcare policies, will help in ameliorating delays in patient presentation, with its associated advanced disease stages, and promote referral to foundations that can further assist with costs of diagnostics and treatment.

At the level of hospitals, investment in the needed number of pediatric cancer referral centers – based on population cancer case estimates and geographical distribution - would help create the multidisciplinary expertise and infrastructure for supportive care that are necessary for improved outcomes. Criteria for pediatric oncology treatment capabilities will establish the networks and required infrastructure at hospitals planning to treat pediatric oncology patients [41]. This, in addition to clear referral networks, would ensure that pediatric patients with cancer are treated at well-equipped hospitals that have the capacity to serve the national burden of disease, delivering optimal opportunities for survival. Such networks would also facilitate collaboration and training among primary and specialist centers to reduce rates of misdiagnoses in the primary healthcare setting.

For such interventions, well-designed national registries that include demographic and outcome data are essential to both identify the most

significant gaps, as well as measure impact of interventions in healthcare delivery re-structuring over time. Such registries must function under Governmental mandates in order for them to be comprehensive and effective.

It is important to keep in mind that the identified barriers are common to most other low- and middle-income countries. As previously discussed by Magrath et al. [42], essential strategies must include changes in public health policies, a focus on training of healthcare specialists and multidisciplinary teams, improved diagnostic, treatment, and supportive care capabilities, and raising awareness and advocacy through NGOs. In addition, local and clinically meaningful research including implementation studies will be needed for further improvement of models of cancer care delivery in the region and other LMICs [43]. These changes, though major, can be introduced stepwise with the collaboration among all relevant stakeholders, with an anticipated positive effect not only for the children and their families, but also society and even economic return considering the gained economically productive person-years [44]. Platforms such as the POEM group can play an important role in facilitating national as well as transversal programs to improve infrastructure, promote knowledge transfer and regional training. In addition, advocacy efforts to improve cancer awareness, commitment to treatment, and promote NGO support in financially vulnerable societies, have the potential to greatly accelerate improving treatment outcomes.

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#### CRedit authorship contribution statement

**Maya Basbous:** Data curation, Formal analysis, Writing - original draft. **Mazin Al-Jadiry:** Data curation, Visualization, Writing - original draft. **Asim Belgaumi:** Data curation, Visualization, Writing - original

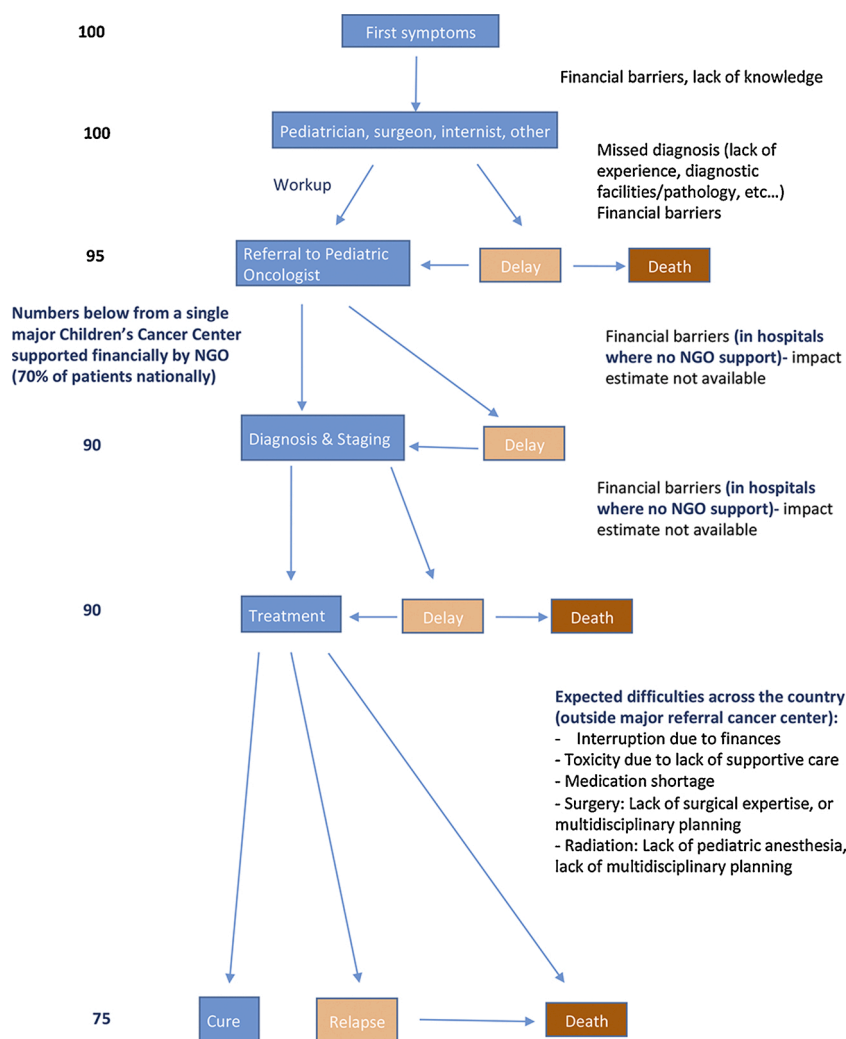


Fig. 5. Pathway of childhood cancer care in Jordan: patient number estimates based on professional personal experience, single institution registry data, and publications.

draft. **Iyad Sultan:** Data curation, Visualization, Writing - original draft. **Alaa Al-Haddad:** Data curation, Visualization, Writing - original draft. **Sima Jeha:** Funding acquisition, Visualization, Writing - original draft. **Raya Saab:** Conceptualization, Data curation, Formal analysis, Visualization, Supervision, Writing - original draft, Writing - review & editing.

**Appendix A. Supplementary data**

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.canep.2020.101727>.

**References**

[1] M.M. Hudson, M.P. Link, J.V. Simone, Milestones in the curability of pediatric cancers, *J. Clin. Oncol.* 32 (2014) 2391–2397, <https://doi.org/10.1200/JCO.2014.55.6571>.  
 [2] C. Rodriguez-Galindo, P. Friedrich, L. Morrissey, L. Frazier, Global challenges in pediatric oncology, *Curr. Opin. Pediatr.* 25 (2013) 3–15, <https://doi.org/10.1097/MOP.0b013e32835c1cbe>.  
 [3] W.T. Johnston, F. Erdmann, R. Newton, E. Steliarova-Foucher, J. Schüz, E. Roman, Childhood cancer: estimating regional and global incidence, *Cancer Epidemiol.* (2020), <https://doi.org/10.1016/j.canep.2019.101662>.  
 [4] N. Bhakta, L.M. Force, C. Allemani, R. Atun, F. Bray, M.P. Coleman, E. Steliarova-Foucher, A.L. Frazier, L.L. Robison, C. Rodriguez-Galindo, C. Fitzmaurice, Childhood cancer burden: a review of global estimates, *Lancet Oncol.* 20 (2019) e42–e53, [https://doi.org/10.1016/S1470-2045\(18\)30761-7](https://doi.org/10.1016/S1470-2045(18)30761-7).  
 [5] T. Seah, C. Zhang, J. Halbert, S. Prabha, S. Gupta, The magnitude and predictors of therapy abandonment in pediatric central nervous system tumors in low- and

middle-income countries: systematic review and meta-analysis, *Pediatr. Blood Cancer* 66 (2019), <https://doi.org/10.1002/psc.27692>.  
 [6] R. Papyan, G. Tamamyian, S. Danielyan, A. Tananyan, A. Muradyan, R. Saab, Identifying barriers to treatment of childhood rhabdomyosarcoma in resource-limited settings: a literature review, *Pediatr. Blood Cancer* 66 (2019), <https://doi.org/10.1002/psc.27708>.  
 [7] S. Gupta, M. Wilejto, J.D. Pole, A. Guttmann, L. Sung, Low socioeconomic status is associated with worse survival in children with cancer: a systematic review, *PLoS One* 9 (2014), <https://doi.org/10.1371/journal.pone.0089482>.  
 [8] F. Bray, J. Ferlay, M. Laversanne, D.H. Brewster, C. Gombe Mbalawa, B. Kohler, M. Piñeros, E. Steliarova-Foucher, R. Swaminathan, S. Antoni, I. Soerjomataram, D. Forman, Cancer Incidence in five Continents: inclusion criteria, highlights from Volume X and the global status of cancer registration, *Int. J. Cancer* 137 (2015) 2060–2071, <https://doi.org/10.1002/ijc.29670>.  
 [9] E.R. Abdelkhalik, L.M. Sherief, N.M. Kamal, R.M. Soliman, Factors associated with delayed cancer diagnosis in Egyptian children, *Clin. Med. Insights Pediatr.* 8 (2014), <https://doi.org/10.4137/cmpep.s16413>.  
 [10] S. Abdelmabood, S. Kandil, A. Megahed, A. Fouda, Delays in diagnosis and treatment among children with cancer: Egyptian perspective, *East. Mediterr. Health J.* 23 (2017) 422–429, <https://doi.org/10.26719/2017.23.6.422>.  
 [11] H.A. Hafez, R.M. Soliaman, D. Bilal, M. Hashem, L.M. Shalaby, Early deaths in pediatric acute leukemia: a major challenge in developing countries, *J. Pediatr. Hematol. Oncol.* 41 (2019) 261–266, <https://doi.org/10.1097/MPH.0000000000001408>.  
 [12] REPUBLIC OF LEBANON Ministry of Public Health, 2005, pp. 1–69 (accessed April 18, 2020), <https://www.moph.gov.lb/en/Pages/8/19526/national-cancer-registry>.  
 [13] R. Saab, Z. Merabi, M.R. Abboud, S. Muwakkit, P. Noun, G. Gemayel, E. Bechara, H. Khalifeh, R. Farah, N. Kabbara, T. El-Khoury, R. Al-Yousef, R. Haidar, S. Saghie, T. Eid, S. Akel, N. Khoury, L. Bayram, M.J. Krasin, S. Jeha, H. El-Solh, Collaborative pediatric bone tumor program to improve access to specialized care:

Table 6

Summary of published literature relating to barriers, treatment, and outcome of common childhood cancers in Pakistan\*.

Author (Year), Hospital, City	Year	N	Age	Tumor type	Outcome	Notes
Siddiqui (2018), Indus Children Cancer Hospital, Karachi	2014–2016	821	0–18 years	All cancers	22% abandoned. 46% abandoned in brain tumors, 31% in solid tumors	Tumor type, rural profession, and lives outside city correlated with abandonment
Amjad (2019), SKMCH, Lahore	2015–2017	150	1–15 years	ALL	15% died: 86% due to sepsis	High-Risk 20%
Asim (2011), SKMCH, Lahore	2001–2005	304	1–18 years	ALL	24% died: 53% in induction, 44% in remission, 3% before therapy	85% deaths due to infection. 11% deaths due to hemorrhage
Jabeen (2016), Children's Cancer Hospital, Karachi	2004–2009	255	1–17 years	ALL CNS + 14%	Deaths 19% in induction, 8% in remission. 7% abandoned. 5-year OS 45%	56% malnourished. No risk stratification. Deaths due to infection
Iqbal (2015), Multiple cities	2004–2013	188	1–15 years	B-cell ALL CNS + 6.4%	2% toxic death. 3-year OS 32%, RFS 18%	BCR-ABL in 48% MLL in 18%
Fadoo (2015), multiple hospitals	2009–2012	646	0–18 years	ALL	Abandonment 13%, Induction death 11%	
Mushtaq (2013), AKU, Karachi	1997–2006	121	<15 years	ALL	12% abandoned, 16% died. EFS 63%, OS 65%	Infection most frequent cause of death
Fadoo (SIOP2018), AKU, Karachi	2009–2012	45	1–10 years	ALL	5-year EFS: 87%	
Ul-Ain (SIOP2019), Children's Hospital Lahore	NA	247	1–16 years	ALL	58% deaths were toxic, 36% of relapse, 6% of disease	Common causes of death: sepsis, bleeding, drug toxicity
Anwar (SIOP2017), Children's Hospital Lahore	2009	198		ALL High-risk 60%, CNS + 7%	40% completed. 22% abandoned, 19% died, 15% relapsed	76% of relapses occurred while on treatment
Fadoo (2012), AKU, Karachi	2000–2007	37	0–15 years	AML	62% treated: 30% died (19% disease, 11% toxic)	
Jabbar (SIOP 2018), The Indus Hospital, Karachi	2013–2017	244	1–17 years	AML	Abandonment 9%, toxic death 33%, relapse 25% EFS 35%	
Faizan (2018), Children's Hospital Lahore	2012–2014	73	5–16 years	NHL Stage III: 91% Stage IV: 8%	66% completed, 22% died, 7% abandoned, 5% relapsed	Burkitt 44% B-cell 14% Lymphoblastic 36%
Rehman (SIOP 2019), SKMCH, Lahore	2012–2016	286	1–16 years	B-Cell NHL: Stage III: 57% Stage IV: 27%	60% CR. 31% died during therapy. 2-year OS 66%, EFS 60%	52% deaths due to colitis. Burkitt in 68%
Faizan (2013), Children's Hospital Lahore	2008–2012	50		Hodgkin Stage III 40% Stage IV 50%	84% remission, 10% died, 2% relapsed, 4% abandoned	Short follow-up. Bone marrow + in 46%
Khan (SIOP2019), The Indus Hospital, Karachi	2013–2017	209	1–17 years	Hodgkin Stage III: 41% Stage IV: 32%	OS 89%; EFS 85%	Chemotherapy +/- radiation
Fatima (SIOP2018), SKMCH, Lahore	2015–2016	150	2–15 years	Hodgkin, 86% Stage III and IV	17% abandoned 16% died (disease/sepsis)	Bone marrow positive in 60%
Ashraf (SIOP2012), Children's Cancer Hospital, Karachi	2000–2009	99	3–20 years	Hodgkin, 37% high-risk, BM+ 5%	6% relapse/progression, 3% died (2/3 infection), EFS 92%, OS 97%	Chemotherapy +/- radiation
Islam (2013), Al-Shifa Trust, Rawalpindi	2006–2009	139	0–4 years	RBL Group E: 76%	Enucleation/ exenteration 78% eyes	16% lost to follow-up within one year. 66% tumor-free
Adhi (2018), Dow University, Karachi	1997–2012	295	0–22 years	RBL 11% Stage IV	Chemotherapy 81% Enucleation 41% Exenteration 3%	20% optic nerve involved on initial imaging
Ahmad (SIOP 2018), Children's Hospital Lahore	2014–2017	150	0–5 years	RBL Optic nerve+ 53%, CNS + 22%	22% abandoned upfront, 44% later. 10% died, 8% relapsed, 7% palliation. 68% enucleation	41% refused surgery. Chemotherapy late in 40%. 22% focal and radiotherapy
Zia (SIOP2018), The Indus Hospital, Karachi	2013–2017	140	0–5 years	RBL Stage IV 24%	17% abandoned upfront 59% on active treatment 24% on palliation	
Imam (SIOP2017), NICH, Karachi	2007–2015	176	0–10 years	RBL Stage IV 32%, CNS + 22%	24% referred with tumor recurrence after primary enucleation	Mean time 12 months between first symptoms and oncology referral
Alam (SIOP2013), Children's Cancer Hospital, Karachi	2007–2012	93	0–10 years	RBL, Stage IV 13%	44% abandoned, 13% palliation only, 36% died. OS 33%	
Naz (SIOP2013), SKMCH Lahore	2007–2011	134	0–10 years	RBL	41% abandoned, 10% died	6% of eyes salvaged
Khan (SIOP2019), SKMCH Lahore	2017–2018	24	NA	Ewing sarcoma	Septic death 12%, Relapse 12%. Toxic cardiac failure 4%	Limb-salvage 38% Amputation 17% Radiation 46%
Resham (SIOP 2018), AKU, Karachi	2005–2015	134	1–16 years	Ewing sarcoma 29% Stage IV	5-year EFS 20% 5-year OS 58% (loc), 42% (met)	26% abandoned upfront, 14% later, 26% died
Resham (SIOP 2018), AKU, Karachi	2005–2015	134	1–16 years	Osteosarcoma, 37% Stage IV	72% abandoned upfront 29% later, 5-year OS 31%, EFS 20%	Multiple regimens. 18% no chemotherapy. 64% amputation.
Syed (SIOP2017), SKMCH, Lahore	2005–2014	225	0–18 years	Osteosarcoma, Localized 82%	34% abandoned, 20% progressed	19% died (progression, infection, cardiac)
Resham (SIOP 2018), 2 hospitals, Karachi	2005–2015	153	1–16 years	RMS Stage IV: 19%	27% abandoned, 37% died during treatment. 5-year OS 58%; EFS 35%	50% of patients either did not start or abandoned therapy
Fadoo (SIOP2017), AKU, Karachi	2005–2015	43	NA	Sarcoma: 26% Stage IV	5-year EFS 43%, OS 55%. Progression 23%	bone 63%. Minimal to no therapy: 14%
Khan (SIOP 2013), SKMCH, Lahore	2007–2011	78	NA	Wilms Stage IV 40%	30% abandoned, 26% died	19% malnourished, 7% toxic death
Anwar (SIOP 2016), Children's Hospital Lahore	2009–2013	175	NA	Wilms, Stage IV 21%	22% abandoned, 42% completed, 11% died, 5% relapsed	Abandonment major factor affecting outcome
Islam Nasir (2016), SKMCH, Lahore	2006–2014	207	0–18 years	Germ Cell Stage IV 12%	Relapse 12%, Abandoned 26%, 5-year OS 45%	
Ahmad (SIOP 2018), Children's Hospital Lahore	2013–2017	90	NA	Gonadal: Stage III: 41% Stage IV: 45%	8% abandoned 15% died	9% had recurrence before being referred for chemotherapy

(continued on next page)

Table 6 (continued)

Author (Year), Hospital, City	Year	N	Age	Tumor type	Outcome	Notes
<i>Ahmad (SIOP 2017), Children's Hospital Lahore</i>	2015–2016	70	0–9 years	Neuroblastoma Stage III: 22% Stage IV: 78%	19% abandoned, 24% died, 10% palliation only	74% had to travel more than 100 km for care. 40% completed therapy
<i>Mehmood (SIOP 2017), SKMCH, Lahore</i>	2001–2010	76	NA	Medullo-blastoma, 42% M+	5-y OS 80% with radiotherapy, 40% without	Multiple treatment regimens
<i>Hamid (SIOP2013), Children's Cancer Hospital, Karachi</i>	2009–2013	100	0–18 years	Brain tumors	37% abandoned, 40% palliation, OS 19%	15% gross resection, 28% radiation, 9% chemotherapy

\* SIOP abstracts in italics, published articles in regular font.

N: number of patients, ALL: acute lymphoblastic leukemia, CNS: central nervous system, OS: overall survival, RFS: relapse-free survival, EFS: event-free survival, AML: acute myeloid leukemia, NHL: non-Hodgkin lymphoma, RBL: retinoblastoma, RMS: rhabdomyosarcoma.

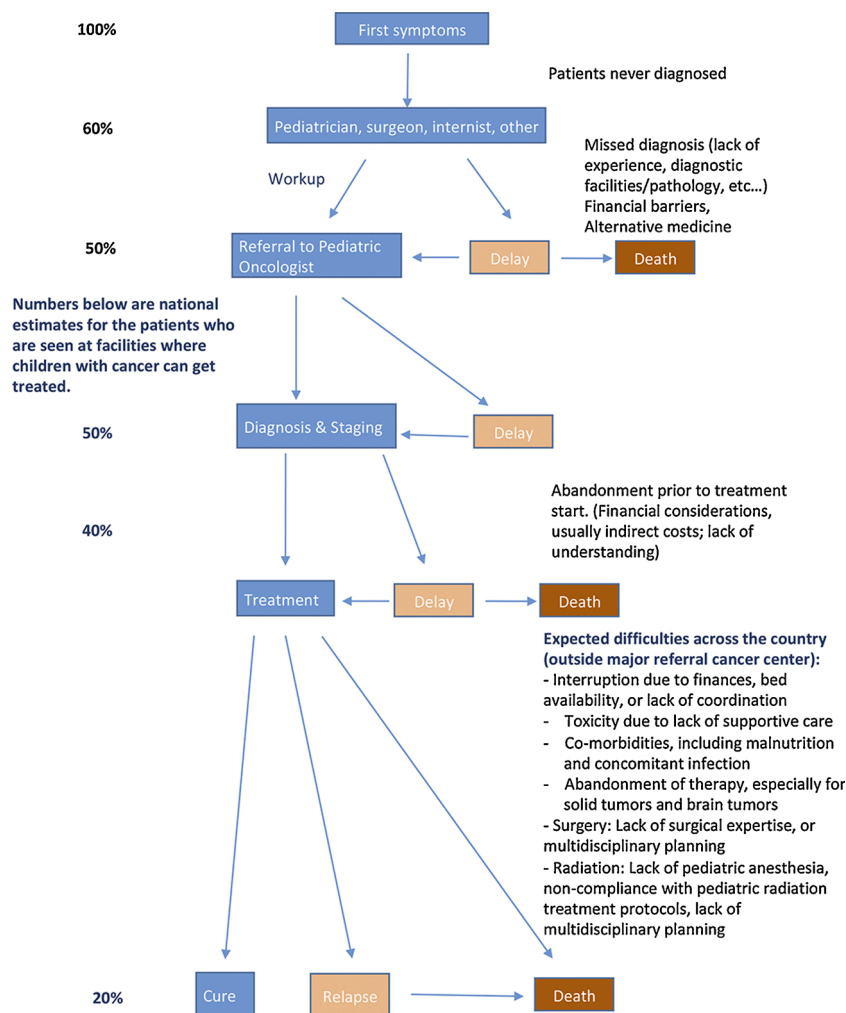


Fig. 6. Pathway of childhood cancer care in Pakistan: patient number estimates based on professional personal experience, single institution registry data, and publications.

an initiative by the Lebanese Children's Oncology Group, *J. Glob. Oncol.* 3 (2017) 23–30, <https://doi.org/10.1200/jgo.2016.003103>.

[14] C. Al-Haddad, Z. Bashour, L. Farah, L. Bayram, Z. Merabe, R. Ma'luf, R. Alameddine, T. Eid, F. Geara, M. Wilson, R. Brennan, S. Jeha, K. Ghanem, R. Al Yousef, R. Farah, P. Noun, N. Yassine, A. Inati, S. Muwakkat, M. Abboud, N. Tarek, D. Hamideh, R. Saab, Establishment of a formal program for retinoblastoma: feasibility of clinical coordination across borders and impact on outcome, *Pediatr. Blood Cancer* 66 (2019), <https://doi.org/10.1002/pbc.27959>.

[15] N. Alwan, D. Kerr, Cancer control in war-torn Iraq, *Lancet Oncol.* (2018), [https://doi.org/10.1016/S1470-2045\(18\)30135-9](https://doi.org/10.1016/S1470-2045(18)30135-9).

[16] P. Cohen, P. Friedrich, C. Lam, S. Jeha, M.L. Metzger, I. Qaddoumi, P. Naidu, L. Faughnan, C. Rodriguez-Galindo, N. Bhakta, Global access to essential medicines for childhood cancer: a cross-sectional survey, *J. Glob. Oncol.* (2018) 1–11, <https://doi.org/10.1200/jgo.18.00150>.

[17] S.A. Al-Hadad, A.M. Testi, M.F. Al-Jadiry, H.H. Ghali, M.L. Moleti, S. Mohamed, A. F. Al-Darraj, S.A. Al-Badri, R.M. Al-Saeed, A. Piciocchi, Pediatric acute lymphoblastic leukemia (all), 17-year experience at Children Welfare Teaching Hospital (CWTH), Baghdad, Iraq, *Pediatr. Blood Cancer*, Wiley, 111 River St, Hoboken 07030-5774, NJ, USA, 2019, pp. S138–S139.

[18] A.M. Testi, R. Foa, M.F. Al-Jadiry, M.L. Moleti, S.A. Al-Hadad, J.K. Al-Tae, W. M. Abed, N.A. Ameen, H.H. Ghali, A.F. Al-Darraj, R.M. Al-Saeed, V. Cecinati, A. De Vellis, A. Piciocchi, Incidence and predictors of early treatment-related mortality in pediatric acute lymphoblastic leukemia in Baghdad (Iraq), *Blood* 116 (2010), <https://doi.org/10.1182/blood.v116.21.2132.2132>, 2132–2132.

[19] H. Frangoul, M.F. Al-Jadiry, Y. Shyr, F. Ye, B. Shakhtour, S.A. Al-Hadad, Shortage of chemotherapeutic agents in Iraq and outcome of childhood acute lymphocytic leukemia, 1990-2002, *N. Engl. J. Med.* 359 (2008) 435–437, <https://doi.org/10.1056/NEJMc0803444>.

[20] M.L. Moleti, M.F. Al-Jadiry, W.A. Shateh, A.F. Al-Darraj, S. Mohamed, S. Uccini, A. Piciocchi, R. Foà, A.M. Testi, S. Al-Hadad, Long-term results with the adapted LMB 96 protocol in children with B-cell non Hodgkin lymphoma treated in Iraq:

**Table 7**  
Common barriers to pediatric cancer care across the five countries.

	Egypt	Lebanon	Iraq	Jordan	Pakistan
Financial Barriers throughout diagnosis and therapy	+++	++	+++	++	+++
Abandonment (throughout diagnosis and treatment)	+	-	++	-	++
Lack of parent awareness/ alternative medicine/ taboo	+	-	+	-	++
Co-morbidities (malnutrition, HIV, TB, etc..)	+++	-	+	-	+++
Missed diagnosis (primary healthcare)	++	+	++	+	++
Lack of pathology diagnosis	-/+	-	+	-	+
Medication Shortage	-/+	-/+	++	-/+	+
Lack of Supportive Care	-/+	-/+	++	-/+	++
Lack of effective surgery/ MDT	-/+	-/+	+++	-/+	-/+
Lack of effective radiation oncology/MDT	-/+	-/+	+++	-/+	+
Security and displacement factors	+	+	+++	+	+

Impact tabulated as: none (-), variable across the country with minimal impact in the few major cancer hospitals (-/+), significant impact affecting <25% (+), 26–50% (++) , 51–74% (+++), and >75% (++++) of patients, respectively.

comparison in two subsequent cohorts of patients, *Leuk. Lymphoma* (2019), <https://doi.org/10.1080/10428194.2018.1519810>.

[21] M.L. Moleti, S.A. Al-Hadad, M.F. Al-Jadiry, A.F. Al-Darraj, R.M. Al-Saeed, A. De Vellis, A. Piciocchi, S. Uccini, R. Foà, A.M. Testi, Treatment of children with B-cell non-Hodgkin lymphoma in a low-income country, *Pediatr. Blood Cancer* (2011), <https://doi.org/10.1002/pbc.22905>.

[22] C. Allemani, M.P. Coleman, Cancer survival rates: the CONCORD-2 study - Authors' reply, *Lancet* 386 (2015) 429–430, [https://doi.org/10.1016/S0140-6736\(15\)61443-X](https://doi.org/10.1016/S0140-6736(15)61443-X).

[23] C. Allemani, T. Matsuda, V. Di Carlo, R. Harewood, M. Matz, M. Nikšić, A. Bonaventure, M. Valkov, C.J. Johnson, J. Estève, O.J. Ogunbiyi, Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries, *Lancet* 391 (2018) 1023–1075, [https://doi.org/10.1016/S0140-6736\(17\)33326-3](https://doi.org/10.1016/S0140-6736(17)33326-3).

[24] H. Halalshah, N. Abuirmeilch, R. Rihani, F. Bazzeh, L. Zaru, F. Madanat, Outcome of childhood acute lymphoblastic leukemia in Jordan, *Pediatr. Blood Cancer* 57 (2011) 385–391, <https://doi.org/10.1002/pbc.23065>.

[25] F. Badar, S. Mahmood, Epidemiology of cancers in Lahore, Pakistan, among children, adolescents and adults, 2010–2012: a cross-sectional study part 2, *BMJ Open* 7 (2017), <https://doi.org/10.1136/bmjopen-2017-016559>.

[26] K. Jabeen, M.S. Ashraf, S. Iftikhar, A.F. Belgaumi, The impact of socioeconomic factors on the outcome of childhood acute lymphoblastic leukemia (ALL) treatment in a Low/Middle income country (LMIC), *J. Pediatr. Hematol. Oncol.* 38 (2016) 587–596, <https://doi.org/10.1097/MPH.0000000000000653>.

[27] N. Mushatq, Z. Fadoo, A. Naqvi, Childhood acute lymphoblastic leukaemia: experience from a single tertiary care facility of Pakistan, *J. Pak. Med. Assoc.* 63 (2013) 1399–1404.

[28] M. Khan, S.A. Muhammad, Pediatric classical hodgkin lymphoma-a PET/CT based study from tertiary care center of Pakistan. *Pediatr. Blood Cancer*, Wiley, 111 River St, Hoboken 07030-5774, NJ, USA, 2019, pp. S112–S113.

[29] M. Ashraf, A. Qidwai, Excellent outcome in pediatric Hodgkin disease with treatment primarily based on chemotherapy with ABVD/COPDAC: PC001, *Pediatr. Blood Cancer* 59 (2012).

[30] P. Rehman, R.M. Wali, Clinical Course and outcome of B cell Non-hodgkin lymphoma in children-single institution study from low income Country. *Pediatr. Blood Cancer*, Wiley, 111 River St, Hoboken 07030-5774, NJ, USA, 2019, pp. S266–S267.

[31] M. Faizan, S. Anwar, S. Khan, Demographics and outcome in paediatric non-Hodgkin lymphoma: single centre experience at the Children Hospital, Lahore, Pakistan, *J. Coll. Physicians Surg. Pakistan* 28 (2018) 48–51, <https://doi.org/10.29271/jcpsp.2018.01.48>.

[32] U. Imam, F. Ali, Clinicoradiologic features of retinoblastoma at national institute of child health Karachi, Pakistan. *Pediatr. Blood Cancer*, Wiley, 111 River St, Hoboken 07030-5774, NJ, USA, 2017, pp. S457–S458.

[33] D.E.F. Siddiqui, M.S. Ashraf, S. Iftikhar, A.F. Belgaumi, Predictors of treatment abandonment for patients with pediatric cancer at Indus Children Cancer hospital, Karachi, Pakistan, *Pediatr. Blood Cancer* 65 (2018), <https://doi.org/10.1002/pbc.26818>.

[34] M. Asim, A. Zaidi, T. Ghafoor, Y. Qureshi, Death analysis of childhood acute lymphoblastic leukaemia: experience at Shaikat Khanum memorial cancer hospital and research centre, Pakistan, *J. Pak. Med. Assoc.* 61 (2011) 666–670.

[35] S. Muhammad, A.F. Belgaumi, M.S. Ashraf, S. Akhtar, S. Iftikhar, M.R. Raza, M. Y. Yakoob, Evaluation of baseline cardiac function by echocardiography and its association with nutritional status in pediatric cancer patients at the Indus Hospital

in Karachi, Pakistan, *J. Pediatr. Hematol. Oncol.* 41 (2019) E388–E394, <https://doi.org/10.1097/MPH.0000000000001437>.

[36] A. Mansour, A. Al-Omari, I. Sultan, Burden of Cancer Among Syrian refugees in Jordan, *J. Glob. Oncol.* (2018) 1–6, <https://doi.org/10.1200/jgo.18.00132>.

[37] F.J. Mateen, M. Carone, H. Al-Saedy, S. Nyce, T. Mutuerandu, J. Ghosn, A. Jatoui, Cancer diagnoses in Iraqi refugees, *Acta Oncol. (Madr)* 51 (2012) 950–951, <https://doi.org/10.3109/0284186X.2012.667148>.

[38] R. Saab, S. Jeha, H. Khalifeh, L. Zahreddine, L. Bayram, Z. Merabi, M. Abboud, S. Muwakkit, N. Tarek, C. Rodriguez-Galindo, H. El Solh, Displaced children with cancer in Lebanon: a sustained response to an unprecedented crisis, *Cancer* 124 (2018) 1464–1472, <https://doi.org/10.1002/cncr.31273>.

[39] J. Alawa, O. Hamade, A. Alayleh, L. Fayad, K. Khoshnood, Cancer awareness and barriers to medical treatment among syrian refugees and Lebanese citizens in Lebanon, *J. Cancer Educ.* (2019), <https://doi.org/10.1007/s13187-019-01516-3>.

[40] M. Al Qadire, M. Aljezawi, N. Al-Shdayfat, Cancer awareness and barriers to seeking medical help among syrian refugees in Jordan: a baseline study, *J. Cancer Educ.* 34 (2019) 19–25, <https://doi.org/10.1007/s13187-017-1260-1>.

[41] J.R. Kowalczyk, M. Samardakiewicz, E. Fitzgerald, S. Essiaf, R. Ladenstein, G. Vassal, A. Kienesberger, K. Pritchard-Jones, Towards reducing inequalities: European standards of care for children with Cancer, *Eur. J. Cancer* 50 (2014) 481–485, <https://doi.org/10.1016/j.ejca.2013.11.004>.

[42] I. Magrath, E. Steliarova-Foucher, S. Epelman, R.C. Ribeiro, M. Harif, C.K. Li, R. Kebudi, S.D. Macfarlane, S.C. Howard, Paediatric cancer in low-income and middle-income countries, *Lancet Oncol.* 14 (2013), [https://doi.org/10.1016/S1470-2045\(13\)70008-1](https://doi.org/10.1016/S1470-2045(13)70008-1).

[43] R. Sullivan, J.R. Kowalczyk, B. Agarwal, R. Ladenstein, E. Fitzgerald, R. Barr, E. Steliarova-Foucher, I. Magrath, S.C. Howard, M. Kruger, M.G. Valsecchi, New policies to address the global burden of childhood cancers, *Lancet Oncol.* 14 (2013), [https://doi.org/10.1016/S1470-2045\(13\)70007-X](https://doi.org/10.1016/S1470-2045(13)70007-X).

[44] R. Atun, N. Bhakta, A. Denburg, A.L. Frazier, P. Friedrich, S. Gupta, C.G. Lam, Z. J. Ward, J.M. Yeh, C. Allemani, M.P. Coleman, Sustainable care for children with cancer: a Lancet Oncology Commission, *Lancet Oncol.* 21 (2020) e185–e224, [https://doi.org/10.1016/S1470-2045\(20\)30022-X](https://doi.org/10.1016/S1470-2045(20)30022-X).

[45] A.-J.M. Al-Hadad S., Outcome of acute promyelocytic leukemia patients experience of Children Welfare Teaching Hospital (2010–2015), *Proc. from 7th Int. Symp. Acute Promyelocytic Leuk.* 24–27 Sept. 2017, Rome, Italy, n.d.

[46] A.M. Testi, S.A. Al-Hadad, M.F.F. Al-Jadiry, M.L. Moleti, F. Mandelli, R. Foà, Impact of international collaboration on the prognosis of childhood acute promyelocytic leukemia in Iraq, *Haematologica* (2006).

[47] M.F. Al-Jadiry, A.M. Testi, H.H. Ghali, M.L. Moleti, S. Mohamed, A.F. Al-Darraj, S. A. Al-Badri, R.M. Al-Saeed, A. Piciocchi, W.M. Abed, N.A. Ameen, Acute lymphoblastic leukemia (all) in infants. *Children Welfare Teaching Hospital (CWFTH) Experience*, Baghdad, Iraq, *Pediatr. Blood Cancer* 66 (2019) S239.

[48] M.L. Moleti, S.A. Al-Hadad, M.F. Al-Jadiry, A.F. Al-Darraj, R.M. Al-Saeed, A. De Vellis, A. Piciocchi, S. Uccini, R. Foà, A.M. Testi, Treatment of children with B-cell non-Hodgkin lymphoma in a low-income country, *Pediatr. Blood Cancer* 56 (2011) 560–567, <https://doi.org/10.1002/pbc.22905>.

[49] A. Di Napoli, M.F. Al-Jadiry, C. Talerico, E. Duranti, E. Pilozzi, P. Trivedi, E. Anastasiadou, A.R. Alsaadawi, A.F. Al-Darraj, S.A. Al-Hadad, Epstein-Barr virus (EBV) positive classical Hodgkin lymphoma of Iraqi children: an immunophenotypic and molecular characterization of Hodgkin/Reed-Sternberg cells, *Pediatr. Blood Cancer* 60 (2013) 2068–2072.

[50] S. Uccini, M.F. Al-Jadiry, S. Scarpino, D. Ferraro, A.R. Alsaadawi, A.F. Al-Darraj, M.L. Moleti, A.M. Testi, S.A. Al-Hadad, L. Ruco, Epstein-Barr virus-positive diffuse large B-cell lymphoma in children: a disease reminiscent of Epstein-Barr virus-positive diffuse large B-cell lymphoma of the elderly, *Hum. Pathol.* (2015), <https://doi.org/10.1016/j.humpath.2015.01.011>.

[51] S. Uccini, M.F. Al-Jadiry, C. Cipitelli, C. Talerico, S. Scarpino, A.F. Al-Darraj, S.A. F. Al-Badri, A.R. Alsaadawi, S.A. Al-Hadad, L. Ruco, Burkitt lymphoma in Iraqi children: a distinctive form of sporadic disease with high incidence of EBV+ cases and more frequent expression of MUM1/IRF4 protein in cases with head and neck presentation, *Pediatr. Blood Cancer* 65 (2018), e27399.

[52] M.L. Moleti, M.F. Al-Jadiry, W.A. Shateh, A.F. Al-Darraj, S. Mohamed, S. Uccini, A. Piciocchi, R. Foà, A.M. Testi, S. Al-Hadad, Long-term results with the adapted LMB 96 protocol in children with B-cell non Hodgkin lymphoma treated in Iraq: comparison in two subsequent cohorts of patients, *Leuk. Lymphoma* 60 (2019) 1224–1233, <https://doi.org/10.1080/10428194.2018.1519810>.

[53] S. Uccini, M.F. Al-Jadiry, G. Pepe, S. Scarpino, S.A. Al-Hadad, L. Ruco, PD-L1 expression in pediatric Epstein-Barr virus positive classic Hodgkin lymphoma is not associated with 9p24. 1 amplification, *Pediatr. Blood Cancer* 66 (2019), e27757.

[54] S. Uccini, M.F. Al-Jadiry, G. Pepe, A. Pasquini, A.R. Alsaadawi, S.A. Al-Hadad, A. Di Napoli, C. Tripodo, L. Ruco, Follicular dendritic cells display microvesicle-associated LMP1 in reactive germinal centers of EBV+ classic Hodgkin lymphoma, *Virchows Arch.* (2019), <https://doi.org/10.1007/s00428-019-02605-w>.

[55] H.M. Phelps, M.F. Al-Jadiry, N.M. Corbitt, J.M. Pierce, B. Li, Q. Wei, R.R. Flores, H. Correa, S. Uccini, H. Frangoul, A.R. Alsaadawi, Molecular and epidemiologic characterization of Wilms tumor from Baghdad, Iraq, *World J. Pediatr.* (2018), <https://doi.org/10.1007/s12519-018-0181-3>.

[56] A.H. Younis Toshi Inoshita, Payman Ali Ihsan Saber Al-Hakem, Salih Hussam M, Jaffar Al-Ghobar, Salma Al-Hadad, The aid for Iraqi childhood leukemia patients from Japan, *Poster SIOP ASIA 2015* (2015).

[57] L.F.Y. Al-Kzayer, K. Sakashita, M.F. Al-Jadiry, S.A. Al-Hadad, H.H. Ghali, L.T. N. Uyen, T. Liu, K. Matsuda, J.M.H. Abdulkadhim, T.A. Al-Shujairi, Z.I.I.K. Matti, Analysis of KRAS and NRAS gene mutations in Arab Asian children with acute leukemia: high frequency of RAS mutations in acute lymphoblastic leukemia, *Pediatr. Blood Cancer* (2015), <https://doi.org/10.1002/pbc.25683>.

- [58] L.F.Y. Al-Kzayer, K. Sakashita, M.F. Al-Jadiry, S.A. Al-Hadad, L.T.N. Uyen, T. Liu, K. Matsuda, J.M.H. Abdulkadhim, T.A. Al-Shujairi, Z.I.I.K. Matti, J.G. Hasan, Frequent coexistence of RAS mutations in RUNX1-mutated acute myeloid leukemia in Arab Asian children, *Pediatr. Blood Cancer* (2014), <https://doi.org/10.1002/xbc.25151>.
- [59] L.F.Y. Al-Kzayer, K. Sakashita, K. Matsuda, S.A. Al-Hadad, M.F. Al-Jadiry, W. M. Abed, J.M.H. Abdulkadhim, T.A. Al-Shujairi, J.G. Hasan, H.M.S. Al-Abdullah, M.H. Al-Ani, P.A.I. Saber, T. Inoshita, M. Kamata, K. Koike, Genetic evaluation of childhood acute lymphoblastic leukemia in Iraq using FTA cards, *Pediatr. Blood Cancer* (2012), <https://doi.org/10.1002/xbc.24055>.
- [60] L.F.Y. Al-Kzayer, L.T.N. Uyen, M.F. Al-Jadiry, S.A. Al-Hadad, S.A.F. Al-Badri, H. H. Ghali, N.A. Ameen, T. Liu, K. Matsuda, J.M.H. Abdulkadhim, T.A. Al-Shujairi, Z. I.I.K. Matti, J.G. Hasan, H.M.S. Al-Abdullah, M.H. Al-Ani, Analysis of class I and II aberrations in Iraqi childhood acute myeloid leukemia using filter paper cards, *Ann. Hematol.* (2014), <https://doi.org/10.1007/s00277-014-2007-2>.