

Chapter 26

Pediatric Oncology in the Arab World



Dua'a Zandaki and Iyad Sultan

26.1 Introduction

Childhood cancer represents a unique challenge in medical care. No other disease receives such emotional sympathy from the public. Yet, it remains to be challenging to allocate resources to offer proper therapy. Nowadays, survival rates for the most common childhood cancers surpass 80% in developed countries, while the average survival approximates 20% in resource-limited settings [1].

The Arab League has 22 member countries that have a population of over 420 million, with one-third of them below the age of 15 (140 million, 33%). There is a great heterogeneity in the region of the world. The Gross Domestic Product (GDP) per capita ranges from 631 to 63,281 USD per capita. This is reflected on all other parameters, including infant mortality rate, for example, which ranges from 6 to 74 per 1000 live births (Table 26.1).

The disparities in the level of care exist even within individual countries. Access to care can be readily available for patients who live close to medical centers, while this can be difficult to reach for those living in less privileged areas. The immigrants and non-nationals who reside in some Arab countries may not be able to afford the expensive care of childhood cancer, and a considerable gap continues to exist.

On the other hand, language and cultural background represent a common background that makes collaboration more feasible. The work of Non-Governmental Organizations (NGOs) may use this as a background for fundraising and health

D. Zandaki

Department of Pediatrics Oncology, King Hussein Cancer Center, Amman, Jordan

I. Sultan (✉)

Department of Pediatrics Oncology, Cancer Care Informatics Program, King Hussein Cancer Center, Amman, Jordan

Department of Pediatrics, University of Jordan, Amman, Jordan

e-mail: isultan@khcc.jo

© The Author(s) 2022

H. O. Al-Shamsi et al. (eds.), *Cancer in the Arab World*,
https://doi.org/10.1007/978-981-16-7945-2_26

409

Table 26.1 Selected World Bank indicators of Arab countries [2]

Country	GDP	Anemia (%)	Death by NCD (%)	Hospital beds	Health expenditure (%)	Health exp. per capita	Birth rate	Infant mortality	Children (%)	Population
Algeria	4700	30	79	2	6	256	24	20	31	43,053,054
Bahrain	20,913	30	86	2	4	994	14	6	19	1,641,172
Comoros	1399	48	45	2	5	65	31	48	39	850,886
Djibouti	1343	42	52	1	2	71	21	48	29	973,560
Egypt	3010	32	86	1	5	126	26	17	34	100,388,073
Iraq	5589	24	67	1	4	239	29	22	38	39,309,783
Jordan	3326	31	80	1	8	330	21	13	34	10,101,694
Kuwait	32,702	25	79	2	5	1711	13	7	22	4,207,083
Lebanon	5792	25	89	3	8	686	17	6	26	6,855,713
Libya	8122	29	75	3	6	310	18	10	28	6,777,452
Mauritania	1756	68	37	0	5	54	33	50	40	4,525,696
Morocco	3396	34	84	1	5	175	18	18	27	36,471,769
Oman	15,082	38	80	1	4	678	19	10	22	4,974,986
Qatar	63,282	26	77	1	2	1716	9	6	14	2,832,067
Saudi Arabia	20,542	38	73	2	6	1485	17	6	25	34,268,528
Somalia	N/A	56	30	1	N/A	N/A	42	74	46	15,442,905
Sudan	1724	57	54	1	5	60	32	41	40	42,813,238
Syria	N/A	35	75	1	4	70	23	18	31	17,070,135
Tunisia	4405	29	86	2	7	252	17	14	24	11,694,719
UAE	41,420	27	77	1	4	1817	10	6	15	9,770,529
Palestine	2939	26	N/A	1	N/A	N/A	29	17	39	4,685,306
Yemen	631	84	50	1	5	73	30	44	39	29,161,922

World Bank Data (2); values were provided for the most recent available data entry since 2016, and decimals were rounded to the nearest number. Indicator names were abbreviated to construct the table: GDP, GDP per capita (constant 2010 US\$); Anemia, Prevalence of anemia among children (% of children under 5); Death by NCD, Cause of death by non-communicable diseases (% of total); Hospital beds, Hospital beds (per 1000 people); Health expenditure, Current health expenditure (% of GDP); Health exp. per capita, Current health expenditure per capita (current US\$); Birth rate, Birth rate, crude (per 1000 people); Infant mortality, Mortality rate, infant (per 1000 live births); Children, Population ages 0–14 (% of the total population); N/A, data not available

initiatives that may help countries with fewer resources. The collaboration and sharing expertise are also feasible and can easily extend to successful twinning.

According to GLOBOCAN, it is estimated that 18,114 children were diagnosed with cancer during the year 2020, and 6910 died (Mortality: incidence ratio of 0.38). The annual incidence of childhood cancer in Arab countries ranges from 7.5 per 100,000 children (Djibouti) to 12.8 (Morocco), and variations may be attributed to registration accuracy (Fig. 26.1) [3]. The top five childhood cancers in the Arab World in 2020 are similar to those reported in the rest of the world (Fig. 26.2) [3].

It is noted that major gaps in our knowledge regarding the true burden of pediatric cancer in the Arab world exists. In a scoping review by Gheorghie et al., where all literature from three Arab countries and Turkey were reviewed, it was revealed that much needs to be done to appreciate the impact of this problem [4]. One particular area of concern was the lack of reliable data regarding the outcome of

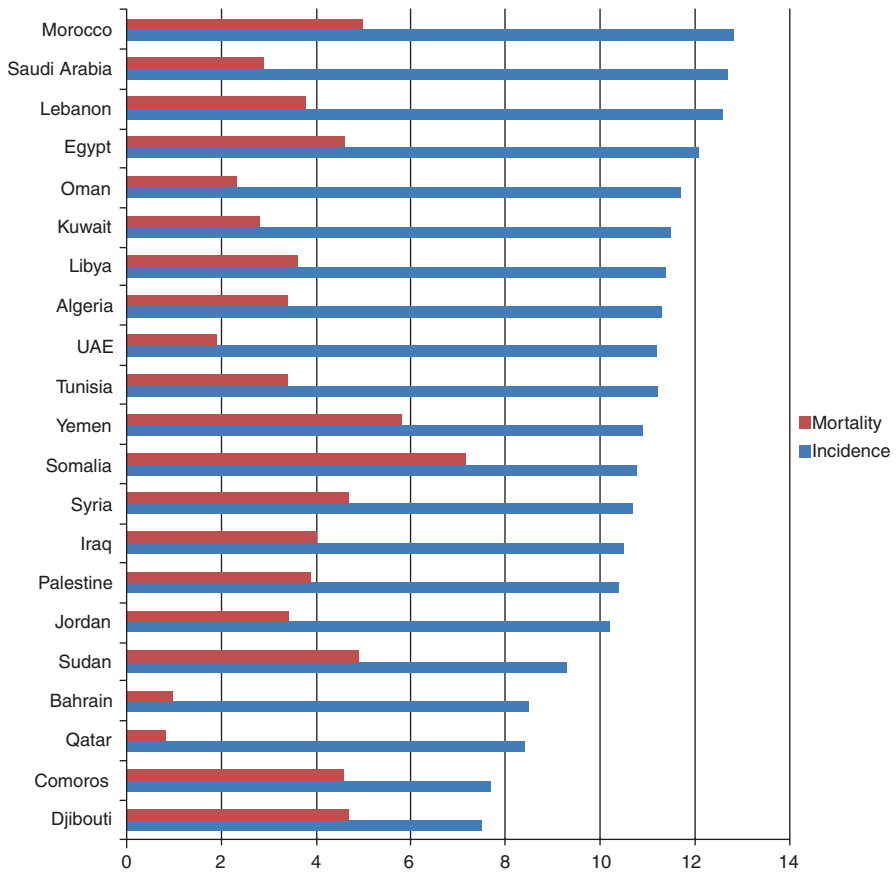
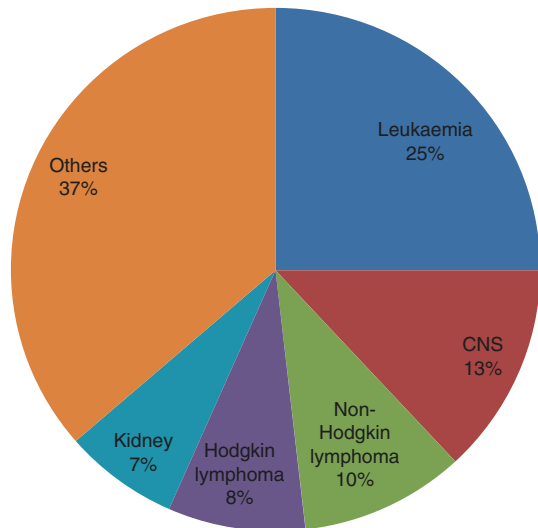


Fig. 26.1 Incidence and mortality rates (per 100,000 children <15 years old) in Arab Countries as estimated by Globocan for the year 2020 [3]

pediatric cancer on national levels. This reflects the need to improve cancer registration and integrate survival data.

Ward et al. developed a microsimulation model to estimate childhood cancer survival across all countries. Their initial estimates were based on CONCORD-2 and CONCORD-3 studies, which were based on data obtained from national cancer registries when it was available [5, 6]. These estimates were then modeled using a computational approach to simulate the effect of different interventions on the outcome of children with cancer. The study estimated that the global 5-year net childhood cancer survival was 37.4% (34.7–39.8%). They found that seven interventions provided small gains in survival, while a comprehensive approach of all policy interventions could raise the global survival of childhood cancer to 80.8%, if fully implemented. The estimates of 5-year net survival in North Africa and West Asia were 30.3% and 56.7%, respectively, which might be increased to 79.2% and 81.4% if all policies adopted [7]. While the estimates for North Africa seem to be alarming, this study was based on data provided by cancer registries, which may overestimate cancer mortality, if diagnosis is not linked properly to survival data. We used the estimates provided in this analysis to draw a map of survival estimates of Acute Lymphoblastic Leukemia (ALL), the most common pediatric malignancy. Figure 26.3 shows the 5- year net survival of ALL estimates using Ward et al. data [7].

Fig. 26.2 A pie chart representing the proportions of the pediatric cancers in the Arab World as provided by Globocan using 2020 estimates [3]



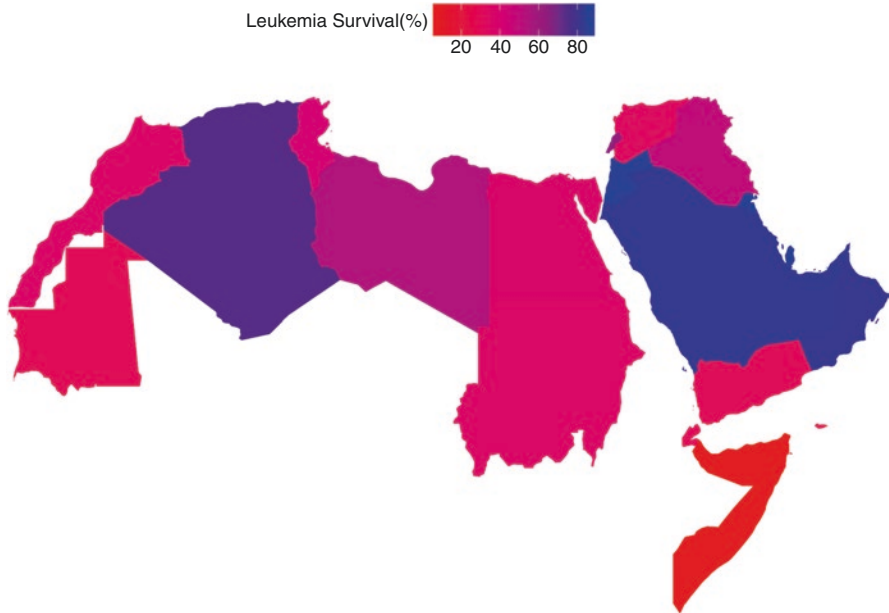


Fig. 26.3 Five-year net survival of Acute Lymphoblastic Leukemia estimates [8]

26.2 Diagnosis Delay and Abandonment

The timely diagnosis of cancer requires the cooperation of parents and pediatricians; parents must seek medical care early on, typically within a month of onset of new persistent symptoms that may initially mimic common childhood illnesses; pediatricians and other practitioners need to be aware of the manifestations of childhood cancer, some can be subtle and require careful history taking and physical examination. This is followed by essential investigations and timely referral to a pediatric oncology unit.

It was suggested that physicians contributed to more delay than parents, and this is consistent with our observations [9]. The delay in diagnosis leads to disease progression, which makes treatment challenging. According to Soliman et al., the rate of delayed diagnosis of retinoblastoma in Alexandria, Egypt was 62%, and it was significantly associated with advanced stage at presentation; 25% of delayed diagnosis was due to misdiagnosis by the first physician, and 21% was due to misjudgment of parents [10].

A study conducted in Egypt to investigate the cancer diagnosis delay in children found that while patient-related causes led to a median delay of 8 days, physician-related causes led to a median of 28 days delay, with a misdiagnosis rate of 40% [11]. As most general physicians are not educated enough about early signs of cancer,

especially in the pediatric age, many families get reassured at their first physician's visit. Even after a physician suspects a serious diagnosis like cancer, confirmation can be challenging, as it requires advanced imaging and biopsy modalities, which are very limited in number and access in many Arab countries. For example, delayed diagnosis in Sudanese children with brain tumors was referred to the fact that there was only one Computed Tomography (CT) machine in the governmental hospital and one Magnetic Resonance Imaging (MRI) machine in the private practice [12, 13].

The initiation and continuation of cancer care are challenging, mainly on the parents' side. Accommodating safe and fast transportation is not always feasible. Many poor families can barely adjust the cost of monthly visits to and from the hospital. Needless to say, this burden has doubled in the COVID-19 era, as many countries imposed curfew hours that limit public transportation. Additionally, the number of hospital visits has increased in number due to the testing for COVID-19 before admissions.

Continuing medical care for children with cancer, which can take as long as 3 years, also requires dedicated human power to accompany the child. Many families find this challenging, as it can lead to job abandonment for parents, and it can lead to negligence towards the child's siblings, especially that the average family size in the Arab world is around 5 in most countries.

One study in Morocco showed that one-third of the children with rhabdomyosarcoma abandoned therapy [14]. A report from Iraq showed that 29 patients with high-grade B- Non-Hodgkin Lymphoma (11% out of 261) abandoned therapy, and that was a major cause for lower outcomes among these patients [15]. The abandonment among patients with Hodgkin Lymphoma in Morocco was also reported to be at 12.5% [16]. A report from Morocco showed that almost 1 out of 5 patients with Wilms tumor abandoned therapy, leading to suboptimal event free survival [17]. A recent report from Jordan showed that 2.5% of families of children with CNS tumors (Total = 473) abandoned therapy while 3% refused a part of treatment [18].

The "My Child Matters" project is a multi-institutional, multi-national initiative. Howard et al. reported their results as 55 institutions were mentored to decrease treatment abandonment, diagnosis delays and toxic death. A median improvement in 5-year survival of 5.1% was noticed. The key elements of successful interventions to overcome these hurdles include strong and sustained local leadership, community engagement, international engagement, capacity building and governmental support [19].

26.3 Pediatric Cancer Treatment

26.3.1 Chemotherapy

Most pediatric malignancies are systemic diseases with a risk of distant spread. Chemotherapy is the sole treatment for most cases of leukemia and lymphoma. Even for solid tumors, chemotherapy is typically essential to reduce volume, facilitate surgery, and prevent local and distant metastasis. Examples include Wilms tumor, germ cell tumors, bone, and soft tissue sarcomas. Autologous and allogeneic transplantation are essential interventions to cure many patients, particularly those

with relapsed leukemia and lymphoma as well as children with neuroblastoma and infants with brain tumors.

Balancing benefits and risks are essential to achieve the best results. Using aggressive protocols that require intensive care may be feasible if needed resources and infrastructure are available. In most cases, adopting regimens designed for High Income Countries (HIC) in Low and Middle Income Countries (LMIC) is not wise, and modifications should be applied to address the unequal health capacity [20].

Each version of the WHO List of Essential Medicines (updated every 2 years) is found to expand the section of antineoplastic drugs. The latest version issued in 2019 contains 21 antineoplastic drugs, and 5 targeted therapies. In our experience, the two essential drugs that suffer from frequent shortages in the Arab World are actinomycin D (essential for rhabdomyosarcoma and Wilms tumor) and L-asparaginase (essential for the treatment of ALL). Concerns regarding the efficacy of generic formulations of these essential drugs deserve careful attention [21]. Data concerning the shortage of essential chemotherapy in the Arab world is sparse. In one report from Iraq, more than half of patients with ALL between 2000 and 2002 received less than 50% of their prescribed chemotherapy. These patients had significantly worse outcomes [22].

In 2001, World Trade Organization (WTO) Members adopted a special Ministerial Declaration at the WTO Ministerial Conference in Doha, termed the Doha declaration, to clarify some terms on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Some of these items included compulsory licensing and parallel importation. These guarantee that LMIC will get access to essential medicines without being subjected to patent-holders [23].

Administering chemotherapy still comes at a significant cost, including the cost of drugs, drug administration, and accommodations needed for inpatient chemotherapy, as well as the cost of treating side effects. For example, Elshahoubi et al. found that Head Start protocol for children with Central Nervous System (CNS) tumors costs approximately 100,000 USD per patient with chemotherapy constituting 40% of the total treatment cost that includes investigations, surgical intervention, radiotherapy, and accommodation. They also found that lower-cost protocols could be used if reliable risk-stratification systems were available, an option that in itself carries an economical burden, due to the need of molecular testing [24].

There are some applicable solutions to cut on treatment costs. For example, treating Ewing sarcoma patients with an outpatient-based interval compression approach was found to save about 21% of the cost in Jordan [25]. Another area of concern is the hesitancy in applying cost-effective evidence-based approaches. For example, despite the well-established fact that cisplatin monotherapy has similar efficacy to the more toxic combination chemotherapy, many institutions continue to use the latter regimen [26].

26.3.2 Radiotherapy

Radiotherapy is an essential part of treating cancer, especially in LMIC, given the higher prevalence of advanced stages at presentation due to delayed diagnosis. The investment in radiotherapy is a continuous one; as it only starts with providing

radiotherapy machines and continues with the need for continuous medical expertise, technical support, and machine maintenance.

According to the Directory for Radiotherapy Centers, the Arab world, whose population averages 420 million, hosts a total of 353 megavoltage machines, 3 kilovoltage machines, and 71 brachytherapy machines. This compares to the USA, of about 75% the Arab population (328 million) that hosts a total of 3727 megavoltage machines, 6 kilovoltage machines, 768 brachytherapy machines, in addition to 37 light ion therapy machines [27].

This scarcity of radiotherapy machines is a major challenge to treating cancer in the Arab world. A report by the commission of Lancet Oncology in 2015 showed that an adequate number of radiotherapy machines was noted in Arab Gulf countries, Jordan and Lebanon [28], while severe shortages were noted in Syria, Iraq, and Yemen. It must be noted that economic challenges are not the only obstacle for establishing this service, as shown by Mousa et al. In their analysis, the number of physicians per 1000 capita was the strongest predictor for the number of machines per capita in the Arab world [29].

The demand for radiation is expected to grow with the increasing incidence of cancer as most Arab populations are undergoing transformation with increased survival. This means that competition for radiation with children may be even worse in the future. A report from Iraq mentions that radiotherapy waiting lists can reach up to 6 months for pediatric patients [30]. This issue deserves immediate attention to improve cancer care for both children and adults.

26.3.3 *Surgery*

Surgical management is essential in treating childhood solid tumors. Surgical expertise is needed to manage complications of therapy as well, e.g., fungal infections, abscesses, typhlitis, and fasciitis. Surgeons aid in getting biopsies for diagnosis and inserting central lines, which requires special expertise in children. Some surgical interventions also require advanced equipment; a good example is neurosurgical procedures, which are currently witnessing huge improvements in HIC with brain labs and robotic surgery. The complexity of postoperative care is perhaps best represented by orthopedic management of limb sarcomas [31].

One under-studied subject here is the competition of the private sector for surgical expertise. In most cases, pediatric oncology units reside in academic institutions or public hospitals where surgeons are paid less and have difficulty getting tools and equipment. This makes retaining expert surgeons challenging. One example is retinoblastoma, where recruiting and retaining qualified ophthalmologists seems to be extremely challenging. One solution would be cooperation with the private sector and special attention to retention plans that attempt to close the financial gap for highly qualified medical staff.

26.3.4 *New Targeted Therapy*

The previously mentioned World Health Organization (WHO) list of essential medicines has been updated in the latest versions to include five targeted therapies: All-trans retinoic acid, dasatinib, imatinib, nilotinib, and rituximab. Although highly effective, targeted therapy comes at considerable financial cost; monthly averages of \$5000 to \$10,000 and annual totals over \$100,000 are common [32]. An example of the financial load would be children with cancers related to Constitutional Mismatch Repair Deficiency (CMMRD), a condition that is more prevalent in the region due to high rates of consanguinity [33, 34]. These patients are now successfully treated with long-term targeted therapy. However, the financial capacity to maintain them for the long run is challenging.

26.3.5 *Multidisciplinary Care*

Coordinating the use of different treatment modalities and the integration of ancillary services, including psychologists, dieticians, social workers, physical therapists and others, is essential in improving outcomes [35, 36]. In our opinion, exchanging medical reports can never be sufficient to treat children with cancer. Direct interactions and discussions with careful coordination, planning, and adjustment of therapy is needed to reach a good outcome. Implementing a successful model of multidisciplinary care can be challenging. Twinning programs can facilitate this and help programs efficiently assemble their teams and initiate their own meetings. Multiple successful examples in the Arab world published their experiences [30, 37, 38].

26.4 Challenges

26.4.1 *Research/Collaboration*

One of the major heralds to cancer research in the Arab world is the lack of meticulous cancer registries. There are few population-based cancer registries, with only 2% to 5% of populations reporting high-quality incidence data [39, 40]. Like other parts of the world, cancer registration needs to deal with issues related to the accuracy of diagnosis, duplication of entries due to patient referral, abandonment of treatment, and accurate registration of death certificates.

Areas of research that deserve special consideration include cost-effectiveness of pediatric cancer care and outcome studies [4]. Cutting-edge research is available in multiple centers in the Arab world, and many centers are already involved in collaborative international trials.

Another major obstacle for research in the Arab world is financial support. According to the United Nations Education, Scientific, and Cultural Organization (UNESCO), total regional gross expenditure on research and development in all Arab countries collectively for 2019 was 19.5 million US dollars compared to 581.5 million dollars in the US alone [41]. Needless to say, political instability may prevent researchers from conducting research as it becomes very challenging to provide resources and secure follow-up [42].

The International Society of Pediatric Oncology- Pediatric Oncology in Developing Countries (SIOP-PODC) is an initiative that the SIOP established in 1990. It has constructed many committees over the years to support SIOP's vision "no child should die of cancer" in LMIC. It now holds an integral part of SIOP's annual meetings, and it has developed many adapted guidelines to approach pediatric cancer in LMIC settings [43]. The SIOP protocols are more welcoming to countries outside Europe, and many Arab countries participate in their trials.

26.4.2 Political Instability

The Arab region has witnessed major political turmoil, especially in the past decade. This was most notable in Syria and Yemen, where local medical data are not available to measure the effect, however, the health crisis is evident in refugees in neighboring countries. Charity is the major source of funding treatment for refugee children with cancer; however, it cannot always be granted, which impairs care in this subset of patients, especially those with advanced disease at presentation.

Turkish investigators conducted a study to compare the survival of Turkish and Syrian refugee children with cancer and found that Syrian refugees had significantly lower survival, independent of cancer type or stage, even though cancer care is financially covered for Syrian refugees in Turkey. The authors attributed this to economic and bureaucratic measures needed to establish the care and seek the first physician, which leads to advanced stages of presentation in this subset [44].

Saab et al. nicely reported the experience of the Childhood Cancer Center of Lebanon (CCCL) in managing Syrian refugees between 2011 and 2017. During this period, 575 Syrian children with cancer presented to their center. Less than one-fifth ($N = 107$) received full coverage for their treatment, while 264 (46%) received consultation only. This highlights the importance of charity and fundraising to cover refugees [45].

Mansour et al. reviewed the burden of cancer among Syrian refugees in Jordan. Around 900 cases of cancer are diagnosed annually among this population (adults and pediatrics). The cost of their treatment using average estimates is more than 22 million USD. This represents an extra challenge on the King Hussein Cancer Foundation (KHCF), which provides financial coverage in most cases [46].

26.4.3 Human Resources

Few guidelines have been issued regarding the human resources required for childhood cancer care in LMIC, including Arab countries. Human resources are often unfortunately neglected while planning for cancer care facilities. Human resources for each country should be planned in accordance with total population and cancer incidence. Unfortunately, resources are allocated to buildings and facilities rather than personnel, which leads to major challenges, including chronically understaffed facilities, and low staff morale, with subsequent poor patient handling.

The National Cancer Institute Division of Cancer Treatment and Diagnosis has issued some guidelines regarding appropriate staff numbers for each LMIC based on population and GLOBOCAN data. They are available on their website [47].

26.4.4 Limited Resources

One would make the uneducated guess that all cancer treatment needs are the direct treatment methods: chemotherapeutic drugs, surgical capacity, inpatient wards, and radiotherapy units, all of which are barely available in most Arab countries. However, cancer treatment is in fact a long and branching process. Pediatric ICU care is a mainstay of cancer treatment, isolation units, nutrition team support, and patient support groups. This is in addition to resources needed for survivors, including continuous medical follow-up, medications like hormone supplement, equipment such as artificial limbs, and management of late chemotherapy effects.

26.4.5 COVID-19

COVID-19 has affected Pediatric Oncology in many ways. A survey was conducted among the heads of pediatric departments in the Pediatric Oncology East and Mediterranean (POEM) group in April 2020. The survey covered multiple hospitals and patient-related aspects that affected overall patient care. It was shown that patient visits were restricted for off-therapy patients in 91% and to the absolute essential on-therapy patients in 50%. LMIC witnessed a delay in administering chemotherapy and doing surgery or radiation by 31% and 46%, respectively. 31% of centers also reported a delay in accepting new cases. Outpatient visits witnessed cancellations in 65% of centers and were challenged due to travel restrictions in 18%. Up to 70% of centers witnessed a decreased staff number, and 29% reported that medical care was affected due to it. As for resource availability, medication and drug supply were in shortage in 50% and 70% of centers, respectively. Bed availability was compromised in 18% of centers due to bed reallocation, and 32% of centers reported a delay in financial approval for cases [48].

26.5 The Global Initiative for Childhood Cancer (GICC)

GICC is an initiative launched by the WHO with the intent of improving survival for childhood cancer. It was launched in 2018 with an aim to make childhood cancer survival reach 60% by 2030, aiming at saving one million more lives. These goals come in line with the 2030 United Nations (UN) Agenda for Sustainable Development, and Non-Communicable Diseases (NCDs) agenda.

By first prioritizing awareness of childhood cancer, and second, supporting countries to offer better cancer care in terms of diagnosis and treatment medicines and technologies, GICC hopes to alleviate the survival gap between upper and lower middle income countries [49].

With the help of host partners, including International Society of Pediatric Oncology (SIOP) and the St. Jude Children's Research Hospital in the USA, GICC is set to accomplish its aims on a national, regional, and global level. Since its establishment in 2018, ten countries have been in the GICC pilot focus group, Morocco being the only Arab country.

The initiative defined its pillars in the term: CURE ALL, to stand for: Center for excellences, Universal health coverage for essential quality services, Regimens and roadmaps for diagnosis and treatment, Evaluation and monitoring, Advocacy, Leveraged financing, and Linked governance. It has also developed many tools to help implement and undertake its pillars, including:

1. Tools to support priority setting, budgeting, and health system planning.
2. Tools to facilitate national dialog in health workforce planning.
3. WHO management guidelines or guidance for six index childhood cancers and supportive care.
4. Access to cancer medicines program.
5. Defined global research priorities.
6. Dataset for cancer registries and monitoring of programs.

All these pillars are being addressed in focused countries through many steps (Table 26.2)

As GICC set its goals in line with 2030 United Nations (UN) Agenda for Sustainable Development, it also is served by the UN sustainable development goals (Table 26.3).

GICC has chosen six main childhood cancers to address, based on their large prevalence all around the world (constitute 50–60% of all childhood cancers), and on their high cure rate with implementation of good treatment practices. These cancers are Acute Lymphoblastic Leukemia, Burkitt lymphoma, Hodgkin lymphoma, Retinoblastoma, Wilms tumor, and low-grade glioma.

Table 26.2 Steps of implementing GICC pillars in focus countries [49]

	Phases of country action			
	Assess	Plan, cost, & finance	Implement	Monitor and modify
CURE ALL core projects				
Analysis of cancer health system	x			
National Cancer Control strategy development/implementation		X	X	X
Implementation of cancer workforce training packages			X	
National network and referral pathway strengthening			X	
Defining national standards and guidelines for index cancers	x		X	
Essential medicines and technologies strengthening, including via UN	x	X	X	X
Economic analysis and benefit packages review of cancer	x	X		
Strengthening and linking cancer registries (population- and hospital-based)	x	X	X	X
Country dashboard for childhood cancer monitoring	x			X
Local/regional advocacy portfolios: case studies, awareness campaigns			X	X

Table 26.3 GICC goals are in line with 2030 United Nations (UN) agenda for sustainable development goals [49]

UN SDG No. 1	Financial protection from catastrophic illness like cancer reduces poverty
UN SDG No. 2	Reducing hunger and malnutrition improves childhood cancer outcomes
UN SDG No. 3	Investing in childhood cancer supports the attainment of multiple health-related targets
UN SDG No. 4	Educational services needed for children with cancer requiring prolonged hospitalization
UN SDG No. 5	Promote access to care that is not discriminatory against girls and enables mothers and families
UN SDG No. 6	Universal access to clean water and sanitation can reduce rates of infection-related complications
UN SDG No. 8	Investing in diverse occupation required for care stimulates local economic growth and employment
UN SDG No. 10	Promote access to care for all communities to reduce catastrophic health expenditure and inequalities
UN SDG No. 16	Investing in child health promotes social stability and reduces exploitation and discrimination
UN SDG No. 17	Multi-sectoral collaboration and international cooperation improve childhood cancer outcomes

26.6 Conclusion

Pediatric oncology faces many challenges in many Arab countries, including diagnosis delay and treatment abandonment, limited research activities, political instability, recruitment and training of human resources, and limited financial support, which all affect the way children with cancer receive their treatment; be it chemotherapy, radiotherapy, surgery, or targeted therapy. The COVID-19 pandemic added more weight to these challenges collectively. Acknowledging and addressing all these challenges is a responsibility that rests upon policy makers and health care workers trying to care for these children. Some suggested solutions are addressing shortages of essential drugs, improving the infrastructure in health care facilities and tailoring evidence-based approaches to develop tolerable and cost-effective treatment regimens personalized to the area. There is a need to establish more twinning programs with advanced centers to quickly improve this discipline. Similar language and cultural backgrounds provide a unique opportunity to collaborate and help in decreasing gaps among countries in the region. We mention the Global Initiative for Childhood Cancer as one of the remarkable global efforts that aim to improve the global outcome of childhood cancer and alleviate the survival gap between high and low middle income countries.

Conflict of Interest Authors have no conflict of interest to declare.

References

1. Gupta S, Howard S, Hunger S, Antillon F, Metzger M, et al. Treating childhood cancers in low- and middle-income countries. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. Disease control priorities, Cancer, vol. 3. 3rd ed. Washington, DC: World Bank. [Internet]. [cited 2020 Nov 23]. Available from: <http://dcp-3.org/chapter/900/treating-childhood-cancers-low-and-middle-income-countries>.
2. World development indicators and other world bank data: WDI-R package (v 2.7.4) <https://cran.r-project.org/web/packages/WDI/index.html>. Accessed 10 May 2021.
3. Globocan 12. International Agency for Research on Cancer Global Cancer Observatory: estimated number of new cases in 2018 ac, both sexes, ages 0–14. <https://gco.iarc.fr/today/home>. Accessed on 1 May 2021
4. Gheorghe A, Chalkidou K, Shamieh O, Kutluk T, Fouad F, Sultan I, et al. Economics of pediatric cancer in Four Eastern Mediterranean countries: a comparative assessment. *JCO Glob Oncol*. 2020;6:1155–70. Epub 2020/07/23
5. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, et al. 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*. 2018;391(10125):1023–75. Epub 2018/02/06
6. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet*. 2015;385(9972):977–1010. Epub 2014/12/04
7. Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Girardi F, Atun R. Global childhood cancer survival estimates and priority-setting: a simulation-based analysis. *Lancet Oncol*. 2019;20(7):972–83. Epub 2019/05/28

8. Ward Z, Yeh J, Bhakta N, Frazier AL, Girardi F, Atun R. Simulation results: global childhood cancer survival. V1 ed. Harvard Dataverse; 2019.
9. Haimi M, Peretz Nahum M, Ben Arush MW. Delay in diagnosis of children with cancer: a retrospective study of 315 children. *Pediatr Hematol Oncol.* 2004;21(1):37–48. Epub 2003/12/09
10. Soliman SE, Eldomyati W, Goweida MB, Dowidar A. Clinical presentation of retinoblastoma in Alexandria: A step toward earlier diagnosis. *Saudi J Ophthalmol.* 2017;31(2):80–5. Epub 2017/06/01
11. Abdelkhalek E, Sherief L, Kamal N, Soliman R. Factors associated with delayed cancer diagnosis in Egyptian children. *Clin Med Insights Pediatr.* 2014;8:39–44. Epub 2014/09/19
12. Elhassan MMA, Osman HHM, Parkes J. Posterior cranial fossa tumours in children at National Cancer Institute, Sudan: a single institution experience. *Child's Nerv Syst.* 2017;33(8):1303–8. Epub 2017/04/23
13. Parkes J, Hess C, Burger H, Anacak Y, Ahern V, Howard SC, et al. Recommendations for the treatment of children with radiotherapy in low- and middle-income countries (LMIC): A position paper from the Pediatric Radiation Oncology Society (PROS-LMIC) and Pediatric Oncology in Developing Countries (PODC) working groups of the International Society of Pediatric Oncology (SIOP). *Pediatr Blood Cancer.* 2017;64(Suppl 5) Epub 2018/01/04
14. Hessissen L, Kanouni L, Kili A, Nachef MN, El Khorassani M, Benjaafar N, et al. Pediatric rhabdomyosarcoma in Morocco. *Pediatr Blood Cancer.* 2010;54(1):25–8. Epub 2009/09/12
15. Moleti ML, Al-Hadad SA, Al-Jadiry MF, Al-Darraj AF, Al-Saeed RM, De Vellis A, et al. Treatment of children with B-cell non-Hodgkin lymphoma in a low-income country. *Pediatr Blood Cancer.* 2011;56(4):560–7. Epub 2011/02/08
16. Hessissen L, Khtar R, Madani A, El Kababri M, Kili A, Harif M, et al. Improving the prognosis of pediatric Hodgkin lymphoma in developing countries: a Moroccan Society of Pediatric Hematology and Oncology study. *Pediatr Blood Cancer.* 2013;60(9):1464–9. Epub 2013/04/23
17. Madani A, Zafar S, Harif M, Yaakoubi M, Zamiaty S, Sahraoui S, et al. Treatment of Wilms tumor according to SIOP 9 protocol in Casablanca, Morocco. *Pediatr Blood Cancer.* 2006;46(4):472–5. Epub 2005/07/22
18. Amayiri N, Bouffet E. Treatment abandonment and refusal among children with central nervous system tumors in Jordan. *Pediatr Blood Cancer.* 2021;68(8):e29054. Epub 2021/05/23
19. Howard SC, Zaidi A, Cao X, Weil O, Bey P, Patte C, et al. The My Child Matters programme: effect of public-private partnerships on paediatric cancer care in low-income and middle-income countries. *Lancet Oncol.* 2018;19(5):e252–e66. Epub 2018/05/05
20. Rodriguez-Galindo C, Friedrich P, Alcasabas P, Antillon F, Banavali S, Castillo L, et al. Toward the cure of all children with cancer through collaborative efforts: pediatric oncology as a global challenge. *J Clin Oncol Off J Am Soc Clin Oncol.* 2015;33(27):3065–73. Epub 2015/08/26
21. Sankaran H, Sengupta S, Purohit V, Kotagere A, Moulik NR, Prasad M, et al. A comparison of asparaginase activity in generic formulations of E.coli derived L- asparaginase: In-vitro study and retrospective analysis of asparaginase monitoring in pediatric patients with leukemia. *Br J Clin Pharmacol.* 2020;86(6):1081–8. Epub 2020/01/12
22. Frangoul H, Al-Jadiry MF, Shyr Y, Ye F, Shakhtour B, Al-Hadad SA. Shortage of chemotherapeutic agents in Iraq and outcome of childhood acute lymphocytic leukemia, 1990–2002. *N Engl J Med.* 2008;359(4):435–7. Epub 2008/07/25
23. The Doha declaration on the tripartite agreement and public health. https://www.who.int/mediacines/areas/policy/doha_declaration/en/. Accessed on 1 May 2021
24. Elshahoubi A, Khattab E, Halalshah H, Khaleifeh K, Bouffet E, Amayiri N. Feasibility of high-dose chemotherapy protocols to treat infants with malignant central nervous system tumors: Experience from a middle-income country. *Pediatr Blood Cancer.* 2019;66(1):e27464. Epub 2018/09/27
25. Elshahoubi A, Alnassan A, Sultan I. Safety and cost-effectiveness of outpatient administration of high-dose chemotherapy in children with Ewing Sarcoma. *J Pediatr Hematol Oncol.* 2019;41(3):e152–e4. Epub 2019/01/05

26. Perilongo G, Maibach R, Shafford E, Brugieres L, Brock P, Morland B, et al. Cisplatin versus cisplatin plus doxorubicin for standard-risk hepatoblastoma. *N Engl J Med.* 2009;361(17):1662–70. Epub 2009/10/23
27. Directory of radiotherapy centers webpage <https://dirac.iaea.org/Home/Equipment>. Accessed on 1 May 2021
28. Atun R, Jaffray DA, Barton MB, Bray F, Baumann M, Vikram B, et al. Expanding global access to radiotherapy. *Lancet Oncol.* 2015;16(10):1153–86. Epub 2015/10/01
29. Mousa AG, Bishr MK, Mula-Hussain L, Zaghloul MS. Is economic status the main determinant of radiation therapy availability? The Arab world as an example of developing countries. *Radiother Oncol.* 2019;140:182–9. Epub 2019/07/20
30. Al-Hadad SA, Al-Jadiry MF, Al-Darraji AF, Al-Saeed RM, Al-Badr SF, Ghali HH. Reality of pediatric cancer in Iraq. *J Pediatr Hematol Oncol.* 2011;33(Suppl 2):S154–6. Epub 2011/10/05
31. Shehadeh A, El Dahleh M, Salem A, Sarhan Y, Sultan I, Henshaw RM, et al. Standardization of rehabilitation after limb salvage surgery for sarcomas improves patients' outcome. *Hematol Oncol Stem Cell Ther.* 2013;6(3–4):105–11. Epub 2013/10/29
32. Targeted therapies: one practice's story. <https://www.ajmc.com/view/targeted-therapies-one-practices-story>. Accessed 12 May 2021
33. Amayiri N, Tabori U, Campbell B, Bakry D, Aronson M, Durno C, et al. High frequency of mismatch repair deficiency among pediatric high grade gliomas in Jordan. *Int J Cancer.* 2016;138(2):380–5. Epub 2015/08/22
34. Khadair-Ahmad O, Al Husaini M, Ghunaimat S, Ismael T, Amayiri N, Halalsheh H, et al. Constitutional mismatch repair deficiency in children with colorectal carcinoma: a Jordanian center experience. *Pediatr Hematol Oncol J.* 2021;6(1):18–21.
35. Cantrell MA, Ruble K. Multidisciplinary care in pediatric oncology. *J Multidiscip Healthc.* 2011;4:171–81. Epub 2011/08/04
36. Fennell ML, Das IP, Clauser S, Petrelli N, Salner A. The organization of multidisciplinary care teams: modeling internal and external influences on cancer care quality. *J Natl Cancer Inst Monogr.* 2010;2010(40):72–80. Epub 2010/04/14
37. Qaddoumi I, Mansour A, Musharbash A, Drake J, Swaidan M, Tihan T, et al. Impact of telemedicine on pediatric neuro-oncology in a developing country: the Jordanian-Canadian experience. *Pediatr Blood Cancer.* 2007;48(1):39–43. Epub 2006/10/27
38. Qaddoumi I, Nawaiseh I, Mehyar M, Razzouk B, Haik BG, Kharma S, et al. Team management, twinning, and telemedicine in retinoblastoma: a 3-tier approach implemented in the first eye salvage program in Jordan. *Pediatr Blood Cancer.* 2008;51(2):241–4. Epub 2008/02/27
39. Copur MS. State of cancer research around the globe. *Oncology (Williston Park).* 2019;33(5):181–5. Epub 2019/05/17
40. Basbous M, Al-Jadiry M, Belgaumi A, Sultan I, Al-Haddad A, Jeha S, et al. Childhood cancer care in the Middle East, North Africa, and West/Central Asia: a snapshot across five countries from the POEM network. *Cancer Epidemiol.* 2021;71(Pt B):101727. Epub 2020/06/06
41. UNESCO institute for statistics, gross domestic expenditure on research and development. Calculation according to current PPP\$. <http://data.uis.unesco.org/?queryid=74#>. Accessed 1 May 2021
42. House DR, Marete I, Meslin EM. To research (or not) that is the question: ethical issues in research when medical care is disrupted by political action: a case study from Eldoret, Kenya. *J Med Ethics.* 2016;42(1):61–5. Epub 2015/10/18
43. Arora RS, Challinor JM, Howard SC, Israels T. Improving care for children with cancer in low- and middle-income countries--a SIOP PODC initiative. *Pediatr Blood Cancer.* 2016;63(3):387–91. Epub 2016/01/23
44. Yagci-Kupeli B, Ozkan A. Syrian and Turkish children with cancer: a comparison on survival and associated factors. *Pediatr Hematol Oncol.* 2020;37(8):707–16. Epub 2020/07/25
45. Saab R, Jeha S, Khalifeh H, Zahreddine L, Bayram L, Merabi Z, et al. Displaced children with cancer in Lebanon: a sustained response to an unprecedented crisis. *Cancer.* 2018;124(7):1464–72. Epub 2018/03/01
46. Mansour A, Al-Omari A, Sultan I. Burden of cancer among Syrian refugees in Jordan. *J Glob Oncol.* 2018;4:1–6. Epub 2018/10/12

47. Human resources needed for cancer control in low & middle income countries. https://rrp.cancer.gov/programsResources/human_resources_needed.htm. Accessed 21 May 2021
48. Saab R, Obeid A, Gachi F, Boudiaf H, Sargsyan L, Al-Saad K, et al. Impact of the coronavirus disease 2019 (COVID-19) pandemic on pediatric oncology care in the Middle East, North Africa, and West Asia region: A report from the Pediatric Oncology East and Mediterranean (POEM) group. *Cancer*. 2020;126(18):4235–45. Epub 2020/07/11
49. Global initiative for childhood cancer. https://www.who.int/docs/default-source/documents/health-topics/cancer/who-childhood-cancer-overview-booklet.pdf?sfvrsn=83cf4552_aM



Dua'a Zandaki is a third-year fellow at the Department of Pediatrics at King Hussein Cancer Center. She is interested in the management of children with relapsed leukemia and is working on establishing CAR-T cell therapy at the center. She is also interested in precision medicine and novel therapeutics used in pediatric oncology.



Iyad Sultan is the Chairman of the Department of Pediatrics at King Hussein Cancer Center in Amman, Jordan. After finishing his fellowship in pediatric hematology-oncology at the Medical University of South Carolina, he joined the center in 2005. He treats mainly children with solid tumors and is working on developing a regimen for patients with high-risk neuroblastoma. Dr. Sultan is interested in global oncology, cancer epidemiology, cancer genomics and bioinformatics. He is an advocate for displaced children with cancer. Recently, he helped establish the Cancer Care Informatics program at KHCC. He is teaching Bioinformatics among the precision medicine modules.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

