

Childhood Cancer Survivors Follow-up: A study from a Third-Level Hospital in a Low-Middle Income Country

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Abstract

Introduction: Childhood cancer (CC) affects 1 in 285 children under the age of 20 in the United States. It has been shown that CC survivors experience short- and long-term effects from the treatment. In this study, the conditions and characteristics of CC survivors treated in the pediatric oncology/Hematology department of a third-level hospital are described.

Methods: This was a retrospective, observational study. Information from the electronic files of the database of the pediatric oncology/hematology department from 2002 to 2017 was revised.

Results: A total of 1,185 childhood cancer survivor files were revised, and the male sex was predominant. The mean age at the diagnosis was 6.6+5.08 years, at the time of the study the mean age, was 14.06+7.02 years. The most frequently reported cancer type was Acute Lymphoblastic Leukemia (22.4%). 93.3% of the patients did not have a relapse. Of the patients, 56.4% were still attending school and 3.4 reported having children.

Discussion: Childhood cancer survivors require follow-up appointments where not only physical progress is assessed, but also long-term effects that may affect social and mental development.

Keywords: Oncology; Pediatric cancer; Survivor; Childhood cancer; Follow-Up.

Introduction

In the United States, 1 in 285 children under the age of 20 is diagnosed with childhood

cancer (CC), with leukemia, malignancies of the central nervous system (CNS), and lymphoma having higher incidences [1].

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Between 0.5% and 4.6% of all morbidity attributable to this cause is caused by CC, and worldwide incidence rates for this condition vary from 50 to 200 per million kids [2].

Between 5,000 and 6,000 new cases of pediatric cancer are identified in Mexico each year. Leukemias represent 52% of all cases, lymphomas represent 10%, and tumors of the central nervous system 10% [3]. Since 1970, survival rates have improved as a result of medical advancements, and today, more than 80% of children who are diagnosed with cancer are still alive and are regarded as having been cured five years after the initial diagnosis [1]. In the Latin American population, it seems that some types of childhood cancers like ALL are secondary to risk factors such as early infection onset, pesticide exposure, and genetic factors. Genetic factors include polymorphisms associated with racial differences too.

Thus, the risk of developing cancer in the early stages of life is a result of the interaction of multiple environmental and biological factors. Recently, poverty has also been associated with higher rates of childhood cancer, but the understanding of this relationship is still in development [4].

Some authors may explain this relationship because of the occupations associated with lower-income populations. For example, groups of Hispanic immigrants are employed in high-risk occupations such as agriculture in which pesticides are used so they are exposed to carcinogenic agents [5]. Also, associated with the diagnosis, it is important to acknowledge the factors that also affect timely diagnoses, such as the age at diagnosis,

sociocultural characteristics, and access to healthcare [6].

It has been shown that CC survivors encounter short- and long-term effects from the treatment; they have an increased risk of morbidity and mortality in adulthood compared to the siblings, which is considered a control group [7,8]. Due to increases in morbidity and mortality rates resulting from long-term effects, it is expected that CC survivors will be followed up by a physician; unfortunately, less than 20% of patients receive this type of care [7,9]. The management goals for patients with CC should focus on three main aspects: 1) reappearance and succeeding malignancies, 2) late outcome of treatment, and 3) prophylaxis [9].

Regarding recurrence and subsequent malignancies, most late recurrences occur 5-10 years after diagnosis (69.1%); likewise, recurrence may rarely occur 30 years after diagnosis [10]. In addition to recurrence, CC survivors have an increased risk of subsequent cancer development. It has been shown that within 30 years of follow-up after the first diagnosis, 20.5% of survivors are diagnosed with second cancer, including 7.9% with malignant cancer [11].

The cancer diagnosis, location, and recommended treatment strategy all influence the likelihood of recurrence and subsequent malignancies [6]. Additionally, factors like female sex, older age at first cancer diagnosis, radiation therapy treatment, and Hodgkin's lymphoma as primary cancer are linked to an increased chance of developing subsequent cancer.

Nonmelanoma skin cancer, which affects 9.1% of CC survivors, and breast cancer, which affects 5% of CC survivors, are the most common subsequent neoplasms [11].

Late effects can occur in any sphere, such as physical, cognitive, and psychosocial [9]. Physical late effects may vary depending on patient characteristics (age, sex, and genetics) and treatment characteristics (type, time, dose, and duration of therapy). The Children's Oncology Group's long-term follow-up guidelines detail late effects according to treatment modality (chemotherapy, radiation, surgery), therapeutic agents (medication, radiation site, dose, surgical procedure), and patient's metabolic response [9].

A 17.5-year follow-up research on CC patients and relatives revealed that CC survivors had a markedly higher risk of contracting any chronic illness. Additionally, survivors had an 8.2 times greater chance of developing a serious or life-threatening chronic disease, such as myocardial infarction, heart failure, early gonadal failure, subsequent neoplasia, or significant cognitive impairment [7].

It has been demonstrated that childhood cancer patients experience neurocognitive changes in a wider range than peers as a consequence of prior therapies on a cognitive level. An overall decline in cerebral capacity and changes in particular areas of working, such as focus, executive function, memory, and visual and motor processing, can be signs of late effects [12,13].

Patients who endure CNS malignancies following neurosurgery and CNS

radiotherapy have lower cognitive performance. 20-40 points may be deducted from general cerebral aptitude [12,14]. In addition, survivors of non-CNS tumors experience neurocognitive impairment in 13-21% of cases. Furthermore, cranial radiation and treatment [systemic or intrathecal] have been linked to cognitive deficits. Methotrexate and dexamethasone are two chemotherapeutic drugs that have been linked to neurotoxicity [13].

Concerning the psychosocial component, CC diagnosis, and therapy can have an influence on the social setting and mental growth, resulting in long-term effects on work, social connections, and psychological standing [9]. Brain tumors, large amounts of cranial radiation, lower age at diagnosis, female sex, and persistent medical conditions are all linked with CC patients having a three times higher likelihood of being jobless as adults [15,16].

Unemployment and lower monetary income can affect independent living, which in turn affects the quality of life of survivors [9]. High levels of social dysfunction have also been shown in patients surviving CC, likely to have fewer friends and spend less time with peers [16].

Due to the age of diagnosis in pediatric patients and the potential longevity among survivors, late consequences of therapy could have a significant impact on the life role-taking abilities as these survivors progressed from adolescence to early adulthood [17].

In Mexico, due to the high demand for patients treated in public hospitals, the

adequate follow-up has not been given, as has been done at the international level, by childhood cancer survivors. Currently, in Mexico, the follow-up of childhood cancer survivors at the adolescent or young adult stages is not standardized.

In this study, the conditions and characteristics of CC survivors treated at the pediatric Oncology/Hematology department of the Civil Hospital of Guadalajara, “Dr. Juan I. Menchaca” are described. The type of CC, age at diagnosis, treatment received, an accumulated dose of chemotherapy, surveillance time, academic performance, social performance, and physical alterations that may be considered late-term effects are taken into consideration for the study.

Methods

This study had an observational, transversal, and retrospective design. The database of the pediatric oncohematology service of the Civil Hospital of Guadalajara, “Dr. Juan I. Menchaca”, and included patients under surveillance for CC who were previously treated at the hospital between 2002 and 2017 were analyzed.

The sample size was calculated using the formula for finite populations, with a confidence index of 95%, and a margin of error of 5%, using maximum variability and given that the size of the population was 1300 files.

The minimum required sample size was at least 297 clinical records that met the selection criteria. The selection criteria were completeness of the electronic file, including the date of diagnosis, the start date of

surveillance, treatment protocol, adverse effects if any, and extension studies relevant to the study. The exclusion criteria were patients who underwent surveillance in the hospital but were previously treated in another center. The information considered from the electronic file for this study was sex, age at diagnosis, type of cancer, type of current activity (work or academic), and information on relapse.

Results

A total of 1,185 electronic files from the CC survivors were included in this study. 54.9% (n=651) of the patients were male patients and 45.1% (n=534) were females.

The mean age at the diagnosis was 6.6+5.08 years, the mean age was 14.06+7.02 years at the time of the study. Regarding the main activity, 56.5% of the sample currently attending school, 8.5% had a job, 1.8% reported that the main activity was home-based, and 6.8% reported that they had no main activity. At the time of the study, the current scholarly level was reported to be 2.7% in preschool, 34.5% in elementary school, 22.3% in junior high school, 12.3% in high school, and 3.5% in bachelor's degrees. Unfortunately, 5.8% reported having dropped out of school, and for 18.8% of the cases, there was no information regarding school activity (Table 1). The most frequent cancer diagnosis was Acute Lymphocytic Leukemia ALL (22.4%), followed by CNS tumors (12.7%) and germ cell tumors (10.4%) (Table 2). Relapse was reported in 79 cases (6.7%), and 1106 cases had no relapse diagnosis at the time of the study.

		Mean	SD
Age	At diagnosis	6.60	5.08
	Current	14.06	7.02
		Count	Percentage
Gender	Male	651	54.9
	Female	534	45.1
Main activity	School	670	56.5
	Work	101	8.5
	House activities	21	1.8
	None	80	6.8
	Unknown	313	26.4
Academic level	Preschool	32	2.7
	Elementary school	409	34.5
	Junior High School	264	22.3
	High School	146	12.3
	Bachelors	42	3.5
	Dropped out	69	5.8
	Unknown	223	18.8

Table 1 Age and academic level of CC survivors.

As for marital status, since the sample was still young according to the mean age, most of the patients were still single (81.9%), it is also reported that 3.6% of the sample had a partner (married/free union) and for the rest of the sample, the information was not available (14.5%). It is important to note that 3.4% of the CC survivors reported having children.

Statistical tests looking for associations and identification of predictor factors for diagnosis and relapse were conducted. The current age and age at diagnosis were analyzed as possible predictors of cancer relapse and there was no significant relationship found ($p=0.247$ and 0.053).

The sex, schooling, and diagnosis were also verified. The sex of the patient did not show an association with the diagnosis, being more frequent in men than in women ($p=0.00$), the

diagnosis did not influence relapse ($p=0.305$) although it was more frequent in patients with ALL, and finally, schooling and occupation were not associated with diagnosis or relapse ($p>0.05$ for all tests).

Discussion

The present study demonstrates that, for this Mexican oncology center, male CC survivors are more frequent than females, and the mean age shows to be 14 years, noting that they are starting or going through adolescence. The most frequently reported cancer is ALL, and this result agrees with previous studies [18,19]. In terms of relapse, it was found that within this population of survivors, 6.7% presented relapse, which tells us that, as is known in the international literature, the chances of long-term survival free of the disease are related to the factor of relapses that the patient presents, as this includes a greater the

number of interventions, treatments, and short or long-term complications [20,21].

Regarding the return of activities to daily life, the population may show a deficit in reintegration into daily life activities, which may be related to a lack of interest in

continuing their studies, intellectual deficits, or the possibility of economic inability to keep up with them. French et al. reported that CC survivors and siblings skip more schools than other children and the predictive factor for this is poor physical health condition only [22].

	Count	Percentage
Appendix cancer	3	0.3
Colon cancer	2	0.2
Nasopharyngeal cancer	1	0.1
Salivary gland tumors	2	0.2
Ewing sarcoma	8	0.7
PNET*	4	0.3
Askin's tumor	4	0.3
Germ cell tumors	123	10.4
Histiocytosis	55	4.6
ALL	265	22.4
Hodgkin lymphoma	112	9.5
Acute myeloid leukemia	42	3.5
Non-Hodgkin lymphoma	94	7.9
Neuroblastoma	30	2.5
Osteosarcoma	36	3.0
Rhabdomyosarcoma	36	3.0
Retinoblastoma	98	8.3
Soft tissue sarcoma	22	1.9
CNS tumors	151	12.7
Hepatic tumors	17	1.4
Renal tumors	80	6.8

Table 2: Type of cancer reported in CC survivors. *PNET: primitive neuroectodermal tumors; ALL: Acute Lymphocytic Leukemia.

Another characteristic studied in this group of patients is interpersonal relationships once they have completed treatment. Several studies have reported that many survivors have problems establishing relationships. In the population, it was found that 81.9% were single; however, some of these survivors were still in the child or adolescent age group, which could explain the prevalence of this status; 3.6% had a couple/relationship, and 14.5% of the population were single. A study by Thompson et al. revealed that although most CC survivors develop social resilience, some may be at greater risk of difficulties in close relationships as adults [23].

It is currently known that oncological treatments can affect the fertility of patients [24,25]; thus, the records of the files were intentionally searched if this variable was found, finding that 3.4% of the survivors had children, 39.6% did not have children, and 57% had no records of this topic. Although it is still early to determine whether CC survivors in this sample may develop fertility issues, this information should be followed up in the upcoming years. In conclusion, interest in CC survival has increased in recent years due to advances in treatments, and thus, increased survival rates. However, many of the drugs used in different treatment protocols may lead to long-term side effects that can affect the physical, social, and mental spheres of daily life in CC survivors.

It is important that health professionals inform patients about the side effects associated with cancer treatment that could occur in the long term to be able to identify them in a timely manner and carry out an appropriate approach if they occur.

The decision of who should be in charge of monitoring the effects is still debated since once the oncological treatment is finished, many patients do not want to return to the institution where they were treated, as it is perceived as the return to a certainly difficult phase.

There is a need to make patients aware of the importance of continuing with follow-up studies and surveys, to keep encouraging a healthy lifestyle to reduce the appearance of other types of diseases as much as possible, not just cancer relapse. The implementation of follow-up clinics after treatment may be a useful long-term strategy to have an adequate and updated registry of childhood cancer survivors and thus study the long-term side effects that the population presents compared to other countries.

Conclusion

Childhood cancer affects a significant percentage of the population, and the costs and effects of treatments prevail in the short and medium term. In medicine, the main objective is to treat, delay or eradicate the disease, however, once the purpose is achieved, the follow-up of survivors is not consistent. The conditions and characteristics of childhood cancer survivors are very different depending on the country and region.

The intention of this study is to describe the characteristics of surviving cancer patients who were treated in a third-level hospital from a low-middle income country such as Mexico and to compare these characteristics with those present in other similar countries.

This will show data regarding sociodemographic characteristics, the types of cancer reported with the highest prevalence, the recidivism rate, schooling, and the development of adult life. In such a way, what is described in this article can serve to identify the strengths or goals to be achieved when comparing the conditions of these patients with those presented in other places.

Conflict of interest

The study's authors affirm that there were no commercial or financial connections that might be viewed as having a possible conflict of interest.

Author contributions

Vega ES, Sanchez ZF, and Romo RH contributed equally to the study. Romo RH designed the study and reviewed the manuscript. Sanchez ZF provided all the

administrative support. Vega ES and Romo RH collected the data. Vega ES performed the statistical analyses and drafted the manuscript. All authors read and approved the final manuscript.

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Data availability statement

On request, datasets are made available: The contributors will make the raw data accessible without undue reservation, which supports the findings of this paper.

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