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Pediatric Cancer Registry at MAHAK Pediatric Cancer Treatment and Research Center: A Single-Center Study from Iran

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ABSTRACT

Background: The childhood cancer registry in Iran is a hospital-based system and there is not any unique and national registry system for pediatric malignancies in Iran. According to the limitations and requirements, this study was designed to clarify the aspect of childhood malignancies in Iran and promote establishing the Iranian national childhood cancer registry system.

Materials and Methods: This cross-sectional longitudinal study was implied on 1500 patients younger than 20-years old diagnosed with any malignancy and admitted at MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) from 2007 to 2014. Data collection was based on a validated questionnaire with three categories including demographic data, clinical data and type of malignancy, and outcomes. Collected data were analyzed using methods for qualitative and quantitative variables (P < 0.05) by SPSS software version 22. The survival rate was calculated by the Kaplan-Meyer method.

Results: This study was implied on 1500 children with a mean age of 6.1 years old. The most common malignancy was acute leukemia (30.7%) followed by central nervous system tumors (27%). At the onset of starting treatment, the rate of conferring with relapse, metastasis, and secondary malignancies was 29%, 19.5%, and 1% respectively. In addition, 52 patients had bone marrow transplantation of whom, 14 cases died. Totally, 42% of patients died and the 3-years, 5-years, and 10-years overall survival rates were $67.7\% \pm 0.01$, $60.3\% \pm 0.01$, and $53.8\% \pm 0.01$, respectively.

Conclusion: Establishing a population-based pediatric cancer registry in Iran is necessary and will be useful for improving the survival rate of mentioned patients.

Keywords: Cancer registry; Iran; Pediatrics; Childhood cancer

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INTRODUCTION

Malignancies in patients younger than 20-years old are rare¹. In 2013 nearly 84% of global childhood cancer (patients younger than 14-years old) was related to the low income and middle-income countries². At that time, the World Bank announced that 27% and 40% of children less than 15-years old existed in middle-income and low-income countries, respectively³.

Researchers, health care providers, and cancer care centers need population-based cancer registry data for their goals. Additionally, cancer registry data could provide information about the outcome, prognosis, survival, and incidence rates of different types of malignancies⁴. Comparative effectiveness researches (CERs) could also be conducted based on this information⁵.

A challenging issue in the pediatric oncology system is designing a pediatric cancer registry with a population scope⁶. Moreover, regional cancer burden estimations can result from populationbased cancer registry data⁷. Hospital-based registry is about patients who get admitted to a single center and enrolled in the registry system of that hospital. Estimating the pediatric cancer incidence rate is a challengeable issue⁸. In spite of improving the surveillance of childhood malignancies, the rate of its mortality is still notable⁹. In Iran, not only there is no unique and national population-based study on childhood cancer registry, but also the majority of pediatric cancer centers report their data on a cancer-type basis. Because of these limitations, some information about the Iranian childhood cancer registry is neglected.

MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) is a referral Non-Governmental Organization (NGO) with multidisciplinary goals for pediatric patients (children younger than 15 years old) with rare and common malignancies. This study was designed to establish a hospital-based childhood cancer registry system in MPCTRC. Our objective was to describe the present and future aspects of childhood malignancies in Iran due to the gathered data in this study. Clarifying the aspects could have a positive impact on decision making, improving the health care system, the outcomes of mentioned patients, and providing a rationale for establishing the pediatric cancer registry system in Iran and even regional countries.

MATERIALS AND METHODS Study design

This cross-sectional longitudinal study was conducted as a hospital-based and noninterventional project in MPCTRC. A total number of 1500 pediatric admitted patients who met the inclusion criteria at MPCTRC were enrolled in the study from April 2007 to May 2014. Those mentioned patients were followed up for 5 years up to 2019.

Population

The inclusion criteria of the study were patients younger than 20 years old with various malignancies who were admitted to MPCTRC for diagnosis and treatment modalities. Other patients older than 20 years old had been excluded from the study. In this regard, our study consisted of 1500 individuals who met the inclusion criteria from 28 April 2007 to 06 May 2014. All of the patients were followed up until 08 Jan 2019.

Informed consent

The study was approved by the Ethical Committee of MPCTRC and Sanofi Iran Company. The study number is DIREG_L_04147. Signed informed consents were obtained from all patients or their parents for using patients' data in the study.

Data collection

A unique questionnaire was designed and validated by the scientific committee of MPCTRC for data gathering. Collected information was categorized into patients' demographics, type of diagnosis, and outcomes.

Patients' demographic information included patients' document number, birth date, age at diagnosis, sex, race, nationality, and birthplace. The outcome category included the last status of the patient (end of treatment, during treatment, or death), the last date of the patient's visit, relapse, or metastasis during the treatment. Moreover, information about the type of bone marrow transplantation of patients had been considered in this study.

Statistical analysis

All data was entered in SPSS software version 22. Quantitative variables were analyzed descriptively by considering mode, median, means, range, and standard deviation. The symmetric analysis for the distribution of data was performed using skewness or kurtosis methods. Qualitative variables were analyzed by confidence interval coefficient and the frequencies. Chi square, spearman, Kendal, Mcnemar chi-square and Pearson chi-square tests (according to the types of the variables) were carried out to find out a possible significant correlation between the variables. The probability value (P) was considered as less than 0.05.

3-year, 5-year, and 10-year Overall Survival (OS) rates were calculated using the Kaplan-Meyer method. The overall survival time was the time between malignancy diagnosis and last call or last visit or the time of death in the patients. Additionally, 3-year Event Free Survival (EFS) rate was calculated considering the time between malignancy diagnosis and the first event including relapse, metastasis, or death.

RESULTS

Patients' demographic information

From 28 Apr 2007 to 06 May 2014, 1500 patients younger than 20 years old were enrolled in this study. Of whom, 1371 patients (91.4%) were Iranian and the rest were from Afghanistan (n=25), Azerbaijan (n=30), Emirate (n=2), Kuwait (n=1), Bahrain (n=1), Iraq (n=69), and Ivory Coast (n=1). Out of Iranian patients, the majority were from Tehran (n=578 cases). Figure 1 shows the distribution of patients from different provinces of Iran.

In considered patients, 861 individuals (57.4%) were male (male to female ratio: 1.3). The mean age of patients at the time of diagnosis was 5.6 ± 0.1 years old. According to the age groups, the majority of patients were related to the age group of 1 to 5 years old (n=569; 37.93%), followed by the age ranges of 5-10 years old (n=423; 28.26%), 10-15 years old (n=320; 21.38%), younger than 1-year-old (n=155; 10.35%) and older than 15 years old (n=33, 2.20%), respectively.

Patient's clinical features

The most common malignancies in considered patients were leukemia (n=460; 30.67%), central nervous system tumors (n=407; 27.13%), sarcoma (n=216; 14.40%), retinoblastoma (n=211; 14.07%), lymphoma (n=120; 8.00%), renal tumors (n=46; 3.07%), neuroblastoma (n=21; 1.40%) and Langerhans cell histiocytosis (n=19, 1.27%).

Flow cytometry results of patients with leukemia revealed that 349 patients contracted Acute Lymphoblastic Leukemia (ALL), 81 patients contracted Acute Myeloid Leukemia (AML) and 30 patients were diagnosed with Chronic Myeloid Leukemia (CML).

Pathology reports of patients with central nervous system (CNS) tumors revealed that there were: 163 patients with glioma (103 low grade glioma, 16 high grade glioma and 44 undifferentiated glioma cells), 128 patients with medulloblastoma, 62 patients with ependymoma, 19 individuals with brain stem tumor, 12 patients with primitive neuroectodermal tumor (PNET) of CNS, nine patients with optic glioma and 14 ones with rare CNS tumors.

Out of enrolled patients with sarcoma, 76 cases had Ewing sarcoma, 62 cases had rhabdomyosarcoma, 49 patients were diagnosed with osteosarcoma and 29 children had non-rhabdomyosarcoma soft tissue sarcoma (NRSTS).

A number of patients (n=66) diagnosed with lymphoma had Hodgkin lymphoma; 34 of whom had non-Hodgkin lymphoma and 21 individuals had Burkitt lymphoma.

Furthermore, in the group of renal tumors, 44 children were diagnosed with nephroblastoma (Wilms' tumor), and two patients had renal cell carcinoma. Table 1 shows the main characteristic issues in considered patients according to their malignancies, while Table 2 is related to the mentioned characteristics based on diagnostic categories.

Outcome

At the time of diagnosis, 53 patients had been admitted with relapse (ALL: n= 23; AML: n=2; CNS

tumors: n=6; Hodgkin Lymphoma: n=5; Non-Hodgkin Lymphoma: n=2; Osteosarcoma: n=5; Ewing sarcoma: n=2; retinoblastoma: n=5; Wilms Tumor (favorable): n=2 and one patient with Langerhans cell histiocytosis).

During the treatment procedure, 437 patients (29.13%) conferred with relapse, 123 individuals (8.20%) experienced metastasis, which was disease progression to distant organs (Table 1). The median time to relapse from diagnosis was 15.5 months (ranged from 1 to 136 months). The median time to metastasis was 12 months (ranged from 1 to 169 months).

Additionally, nine children (1%) developed secondary malignancy and their demographic and clinical characteristics are shown in Table 3.

Bone Marrow Transplantation (BMT)

Totally, 52 children had bone marrow transplantation (autologous transplantation: 33 patients; allogeneic transplantation: 19 cases). The median time from diagnosis to BMT was 36.21 months (ranged from 3 months to 102 months).

Patients who had autologous transplantation had been diagnosed with Hodgkin lymphoma (n=19); retinoblastoma (n=3); sarcoma (n=3); Wilms Tumor (favorable) (n=2); neuroblastoma (n=2); ALL (n=1), AML (n=1); non-Hodgkin lymphoma (n=1) and one patient with CNS tumors. The median time from diagnosis to autologous BMT in these patients was 35.84 ± 4.6 months (ranged from 3 to 99 months).

Patients with allogeneic transplantation were diagnosed with ALL (n=15); AML (n=3) and a case with retinoblastoma. The median time from diagnosis to allogenic BMT was 36.84± 7.9 months (ranged from 5 to 102 months).

Unfortunately, of patients with BMT, 14 died. Pulmonary Graft Versus Host Disease (GVHD) in 3 cases, blood pulmonary in 2 children, sepsis, and relapse were causes of death after BMT. Additionally, six children died in their living cities (not at the MAHAK hospital), and consequently, their cause of death is unknown.

Survival and follow-up

Up to the last follow-up (08 Jan 2019), 615 patients (42.56%) died, of whom 14 children had received BMT (autologous BMT: n=6; allogeneic BMT: n=8). Out of 885 alive patients, 688 children (77.74%) were off treatment without any problem, 164 individuals were referred to their residence cities for continuing treatment and only 33 children were still under

treatment modalities in MPCTRC. The 3-years, 5-years and 10-years overall survival rates of enrolled patients were $67.7\% \pm 0.01$, $60.3\% \pm 0.01$ and $53.8\% \pm 0.01$ respectively. The mean time of follow-up was 4.5 years ± 0.1 . Event Free Survival (EFS) was calculated and results showed that 3-years EFS was $62.5\% \pm 0.25$. The mean time of EFS was 1.2 years ± 0.6 . Table 4 shows the survival rates of patients based on the type of their malignancies.

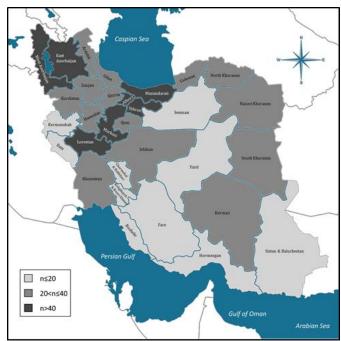


Figure 1: Schematic distribution of Iranian patients based on their living cities (n=1371). Number of patients from each province of Iran who referred to our center are as follows: Tehran:578, Alborz: 98, Mazandaran: 58, West and east Azerbaijan: 49, Lorestan: 47, Markazi: 47, Isfahan: 38, Qom: 37, Gilan: 37, Zanjan: 37,

Khuzestan: 37, Kurdistan: 34, Golestan: 33, Qazvin: 33, Kerman: 29, Khorasan: 26, Hamedan: 25, Ardebil: 21, Semnan: 20, Kermanshah: 17, Yazd: 16, Hormozgan: 16, Ilam: 13, Sistan & Baluchestan: 11, Chaharmahal & Bakhtiari: 9, Bushehr: 3, Fars: 2, Kohgiluyeh & BoyerAhmad: 0.

Renal Langerhans Cell Leukemia **CNS** Tumors Sarcoma Retinoblastoma Lymphoma Neuroblastoma Tumors Histiocytosis [n (%)] Sex of patients 127 (58.7%) 86 (71.67%) 21 (45.65%) 239 (58.72%) 117 (55.45%) 11 (52.38%) 9 (47.37%) Male 251 (54.57%) 209 (45.43%) 168 (41.28%) 89 (41.3%) 94 (44.55%) 34 (28.33%) 25.54 35% 10 (47.62%) 10 (52.63%) Female Age groups (years) 10 (4.62%) • ≤ 1 18 (3.91%) 22 (5.40%) 87 (41.2%) NA 9 (19.57%) 7 (33.33%) 2 (10.52%) • 1-5 195 (42.39%) 156 (38.32%) 42 (19.44%) 130 (54.50%) 20 (35.83%) 20 (43.47%) 10 (47.61%) 11 (57.89%) 71 (32.87%) 9 (19.57%) • 5-10 129 (24.04%) 153 (37.59%) 9 (4.26%) 46 (37.50%) 3 (14.29%) 3 (15.78%) 73 (17.93%) 46 (5.83%) 1 (4.76%) 3 (15.78%) 105 (22.82%) 87 (40.27%) NA^a 5 (10.86%) • 10-15 13 (2.82%) 3 (0.73%) 6 (2.77%) NA 8 3 (6.52%) NA NA ≥ 15 Last status of patient • Off-Treatment 73 (33.79%) 198 (43.04%) 168 (41.27%) 114 (54.02%) 89 (74.17%) 27 (58.70%) 5 (23.81%) 14 (73.68%) During Treatment 2 (0.93%) 28 (6.08%) 1 (0.25%) 1 (4.76%) 1 (5.26%) NA NA NA 16 (7.40%) Referred to their living 37 (8.04%) 41 (10.07%) 52 (24.64%) 8 (6.67%) 4 (8.70%) 3 (14.29%) 3 (15.78%) city for continuing 125 treatment there 197 (42.82%) 197 (48.40%) 45 (21.33%) 15 (32.16%) 23 (19.17%) 12 (57.14%) 1 (5.26%) (57.87%) Death 34 (28.33%) 158 (34.34%) 67 (31.01%) 4 (21.05%) Relapse 76 (18.67%) 80 (37.91%) 10 (21.73%) 8 (38.10%) MTR^b (months) 20 13.5 23 9 16 16 12.5 63 Metastasis 9 (1.95%) NA 52 (24.07%) 10 (4.73%) 5 (4.16%) 13 (28.26%) 7 (33.33%) 1 (5.26%) MTM^c (months) 31 6.5 12 13.5 12 16 8 14 Secondary Cancer 3 2 1 2 NA NA NA 1

Table 1. Demographic and clinical features of considered patients based on the type of malignancy (n=1500)

a: Not Applicable, b: Mean-time of relapse from diagnosis, c: Mean-time of metastasis from diagnosis

Table 2. Demographic and clinical features of considered patients based on the diagnostic categories (n=1500)

	Leukemia			CNS Tumor				Sarcoma				Lymphoma				
	ALL ^a	AML ^b	Gliomac	MBd	EPe	BST ^f	PNET ⁹	OPG	h Rare	Ewing	RMS ⁱ	Osteo j	NRSTS ^k	ΗĽ	NHL ^m	BL
Sex of Patients:																
Female	158	38	79	38	23	10	7	6 3	3	38	18	23	10	17	12	5
Male	190	43	84	90	39	9	5	3	9	38	44	26	19	49	22	16
Age Groups (year):																
 ≤ 1 	11	7	13	2	2	1	0	3	0	1	6	2	1	0	0	0
• 1-5	169	24	61	48	27 24	7	5	4	4	15	20	3	4	8	5	7
• 5-10	94	26	54	57	24	9	3	1	4	27	20	11	13	21	19	7
• 10-15	66	21	34	21	9	2	3	1	3	31	16	31	9	30	9	7
 ≥ 15 	8	3	1	0	0	0	1	0	1	2	0	2	2	7	1	0
Last Status of Patients:																
 OT° 	171	27	72	61	22	1	1	7	4	24	20	13	16	51	20	18
 DT^p 	5	0	0	1	0	0	0	0	0	0	2	0	0	0	0	0
 RLCCT^q 	32	2	17	17	5	1	0	1	0	3	5	3	5	9	0	0
Death	140	52	74	49	35	17	11	1	8	49	35	33	8	6	14	3
Events:																
 Relapse 	127	04	28	04	18	0	2	2	4	25	24	13	F	23	0	0
Metastasis	7	31 2	28 8	21 10	5	2 0	3 2	3 0	0	25 20	24 15	13	5 4	23	9 2	2 0
	'	2	0	10	5	0	Z	0	0	20	15	15	4	3	2	0
Mean Time of Events:																
 MTR^r 								32.								
(months)	24	8.5	11.1	10	17.5	7.5	9.5	52.	20	21	26	24	4	19	15	8
 MTM^s (months) 	31	13	5	7	2	NA ^t	16.5	NA	NA	15	11	18	9	0	24.5	NA

a:Acute Lymphoblastic Leukemia; b: Acute Myeloid Leukemia; c: CNS Gliomas (high grade, low grade or undifferentiated); d: Medulloblastoma; e: Ependymoma; f: Brain stem tumors, g: Primitive neuroectodermal tumor of the CNS; h: Optic pathway glioma, i: Rhabdomyosarcoma; j: Osteosarcoma; k: Non-rhabdomyosarcoma soft tissue sarcoma; l: Hodgkin lymphoma; m: non-Hodgkin lymphoma; n: Burkitt lymphoma; o: off treatment; p: during treatment; q: referred to their living cities for continuing treatment; r: Median-time of metastasis from diagnosis; s: Median-time of relapse from diagnosis; t: Not Applicable. Table 3. Demographic and clinical features of pediatric patients with secondary malignancies (n=8).

	Sex	Dx Age ^a (years)	Type of first DX	SM Age ^ь (years)	Type of Secondary Malignancy	Treatment for Dx ^h	Last status
Case 1	Male	0.9	Retinoblastoma	6.5	AML ^d -non-M3	Chemotherapy	OT ⁱ
Case 2	Male	6.2	ALL ^c	15.5	CNS Tumor- PNET ^e	Chemotherapy	Death
Case 3	Male	8.2	CNS Tumor- Ependymoma	8.2	CNS Tumor-GBM ^f	Chemotherapy and Surgery	Death
Case 4	Female	2.2	Retinoblastoma	10	Osteosarcoma	Chemotherapy	ОТ
Case 5	Female	12.4	Langerhans Cell Histiocytosis	14.8	AML-M1	Chemotherapy and Surgery	RLCCT ^j
Case 6	Female	8.8	ALL	16.2	Mucoepidermoid Carcinoma	Chemotherapy and Surgery	ОТ
Case 7	Female	12	ALL	17.1	CML ^g	Chemotherapy	DT ^k
Case 8	Female	14.1	Ewing Sarcoma	18.8	AML-M4	Chemotherapy and Surgery	Death
Case 9	Female	14	CNS Tumor - Glioma	16	Rhabdomyosarcoma	Chemotherapy and Surgery	Death

a: patient's age at the time of primary malignancy diagnosis; b: patient's age at the time of secondary malignancy diagnosis; c: Acute Lymphoblastic Leukemia; d: Acute Myeloid Leukemia; e: Primitive neuroectodermal tumor of the CNS; f: Glioblastoma Multiform, g: Chronic Myeloid Leukemia; h: Treatment method for curing patient's primary malignancy, i: off treatment; j: during treatment; k: referred to their living cities for continuing treatment;

Table 4: Survival rates of considered patients based on malignancy type

	ALL	CNS Tumors	Sarcoma	Retinoblastoma	Lymphoma	Renal Tumors	Neuroblastoma	Langerhans Cell Histiocytosis
3-years OS ^a	67.3% ± 0.02	58.9 %± 0.02	58.3% ± 0.03	82.5% ± 0.02	86% ± 0.03	77.1% ± 0.06	52.4% ± 0.1	94.7% ± 0.05
5-years OS	60.7% ± 0.02	51.4% ± 0.02	44.4% ± 0.03	76.5 %± 0.03	84.1% ± 0.03	67.5% ± 0.07	46.4% ± 0.1	94.7% ± 0.05
10-years OS	53.1%±0.02	46.9% ± 0.02	36.1% ± 0.03	75.0% ± 0.03	79.1% ± 0.04	60.8% ± 0.09	39.9% ± 0.1	94.7% ± 0.05
3-years EFS [♭]	63.4% ± 0.03	41.8% ± 0.10	47.1% ± 0.02	72.9% ± 0.12	73.7% ± 0.04	71.0% ± 0.19	40.3% ± 0.90	90.0% ± 0.07

a: Overall Survival, b: Event Free Survival

DISCUSSION

A definite population-based cancer registry is required for making decisions about prevention, early diagnosis, and treatment modalities for improving surveillance and decreasing the mortality of pediatric malignancies worldwide¹⁰. rate However, the majority of the Iranian pediatric population with malignancies are not supported by a national childhood cancer registry system to evaluate their incidence, mortality, and morbidity rates. This project was designed as a pilot study of the pediatric cancer registry system at MPCTRC to overlook the mentioned problem and to provide reliable data for a better understanding of childhood cancer in Iran.

Our data analysis revealed that the male to female ratio of considered patients was 1.3 with a mean age of 5.6 \pm 0.1 years old at the time of diagnosis. The Swiss Childhood Cancer Registry (SCCR), which has been established since 1976, registered solid tumors, leukemia, lymphoma, CNS tumors, and LCH in patients younger than 21 years of age¹¹. The validation of the Swiss pediatric cancer registry was started by SCCR in 2007 ¹², all of which were classified according to the 10th version of the International Classification of Diseases (ICD-10) ¹³. A population-based cancer registry designed and conducted from 2001 to 2010 provides vital information about the incidence of any types of malignancy in patients younger than 14 years old

(140.6 per one million individuals annually). Its data showed that the incidence of malignancies in male patients younger than 14 years old were higher than female ones with the same age range (M/F ratio: 1.17). In our study, M/F ratio was 1.3, which means that the proportion of male patients was slightly more. In addition, a study by Shabani et al. reported the national and subnational trends of the Iranian pediatric malignancies from 1990 to 2016. The results of the mentioned study showed an increase in the median age in pediatric patients less than 15 years old from 10.08 in 1990 to 11.9 years old in 2016 ¹⁰. The M/F ratio had remained approximately the same (1.3) for 27 years.

In 2010, the International Classification of Childhood Cancer announced that in European patients less than 15 years old, 34% had leukemia, 23% had brain tumors and 12% had lymphoma. Additionally, at that time, the most common malignancies were ALL, astrocytoma, neuroblastoma, and non-Hodgkin lymphoma¹⁴. Moreover, a one-year-follow-up study from Bihar in 2020 revealed that out of 247 pediatric patients with cancer, 57% and 43% were diagnosed with hematolymphoid and solid tumors, respectively¹⁵. In our study, 31% and 27% of cases were diagnosed with acute leukemia and CNS tumors, respectively, which was approximately the same as the European patients.

In the mentioned 10-year population-based cancer registry, the majority of patients were under age of four years old, amongst whom 36% and 5.3% had leukemia and lymphoma, respectively. The second most frequent malignancy after leukemia was CNS tumors in patients younger than 4 years old ¹. In the study of Shabani et al. from Iran, the majority of patients were related to the age group of one to four years old. The most common malignancies in considered patients were leukemia, lymphoma, retinoblastoma, and CNS tumors. Our findings showed that the majority of patients (nearly 60%) were younger than 5 years old, which was as same as the studies conducted at the regional and global levels. Meanwhile, the most common malignancy was leukemia followed by CNS tumors in this age range.

Population-based cancer registries are necessary for cancer control decisions and estimating cancer burdens¹⁶. They are also fundamental systems for estimating the incidence and survival rates of malignancies¹⁷. Nowadays, pediatric cancer is introduced as the second cause of mortality in children younger than 14 years old with an incidence of 11060 cases and 1190 deaths annually¹⁸. Among all pediatric malignancies, leukemia, CNS tumors, and lymphoma are the most common cancers globally¹⁹. Furthermore, the worldwide 5-year overall survival rate of pediatric patients diagnosed with malignancy has increased from 58% between 1975 and 1979 to 83% between 2003 and 2009 ²⁰. In our study, the overall 5-year and 10-year survival rates were $60.7\% \pm 0.02$. In the Iranian study by Shabani et.al¹⁰, there was not any report of survival to be compared with our existing data.

The most important limitation of this study includes its single-center nature and the small sample size of the Iranian children population. Therefore, a multicenter study or national cancer registry system could provide greater knowledge on this matter. On the bright side, as the MPCTRC is a referral center for pediatric cancer and 1500 children were evaluated in our study during 12 years, the data from this study could be highly reliable and can lead to establishing a national system for the Iranian childhood cancer.

CONCLUSION

Overall, the M/F ratio, the most common age range, and the commonest pediatric cancer types in Iran are similar to other global reports; however, there is a gross disparity between survival rates of childhood cancer, which is reported via hospitalbased registries. Therefore, the authors strongly emphasize on the need for establishing a national pediatric cancer registry system in Iran in order to understand the real trend and profile of incidence and mortality rate of Iranian pediatric cancer. The suggested issue could lead to improving the survival rate of Iranian pediatric patients diagnosed with malignancies.

REFERENCES

1. Steliarova-Foucher E, Colombet M, Ries LA, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. Lancet Oncol. 2017;18(6):719-31.

2. Magrath I, Steliarova-Foucher E, Epelman S, et al. Paediatric cancer in low-income and middle-income countries. Lancet Oncol. 2013;14(3):e104-e16.

3. World development indicators. Available from: https://databank.worldbank.org/source/world-development-indicators.

4. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. J Clin Oncol. 2010;28(15):2625.

5. Hershman DL, Wright JD. Comparative effectiveness research in oncology methodology: observational data. J Clin Oncol. 2012;30(34):4215-22.

6. Fedorovsky JM, Cuervo LG, Luciani S. Pediatric cancer registries in Latin America: the case of Argentina's pediatric cancer registry. Rev Panam Salud Publica. 2017; 41: e152.

7. Robinson D, Sankila R, Hakulinen T, Møller H. Interpreting international comparisons of cancer survival: the effects of incomplete registration and the presence of death certificate only cases on survival estimates. Eur J Cancer. 2007;43(5):909-13.

8. Johnston W, Erdmann F, Newton R, Steliarova-Foucher E, Schüz J, Roman E. Childhood cancer: Estimating regional

and global incidence. Cancer Epidemiol. 2021;71(Pt B):101662.

9. Becker C, Graf N, Grabow D, et al. Early deaths from childhood cancer in Germany 1980-2016. Cancer Epidemiol. 2020;65:101669.

10. Shabani M, Saeedi Moghaddam S, Ataeinia B, et al. Trends of National and Subnational Incidence of Childhood Cancer Groups in Iran: 1990–2016. Front Oncol. 2020;9:1428.

11. Schindler M, Mitter V, Bergstraesser E, Gumy-Pause F, Michel G, Kuehni CE. Death certificate notifications in the Swiss Childhood Cancer Registry: assessing completeness and registration procedures. Swiss Med Wkly. 2015;145:w14225.

12. Mitter VR, Michel G, Wölfli P, et al. Swiss Childhood Cancer Registry: Annual Report 2011/2012. 2013.

13. World Health Organization. (2015). International statistical classification of diseases and related health problems, 10th revision, Fifth edition, 2016. World Health Organization. Available from:

https://apps.who.int/iris/handle/10665/246208.

14. Kaatsch P. Epidemiology of childhood cancer. Cancer Treat Rev. 2010;36(4):277-85.

15. Pandey A, Singh A, Kumar V, et al. Pediatric cancers in Bihar: A retrospective tertiary cancer center study. South Asian J Cancer. 2020;9(1):53.

16. Piñeros M, Znaor A, Mery L, Bray F. A global cancer surveillance framework within noncommunicable disease surveillance: making the case for population-based cancer registries. Epidemiol Rev. 2017;39(1):161-9.

17. Freddie Bray, Ariana Znaor, Patricia Cueva, et al. (2014). Planning and developing population-based cancer registration in low- and middle-income settings. Lyon, France: International Agency for Research on Cancer (IARC Technical Publication No. 43).

18. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7-34.

19. Baliga S, Yock TI. Pediatric Cancer. Hematol Oncol Clin North Am. 2020;34(1):143-59.

20. DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin. 2014;64(4):252-71.