

Incidence trends of germ cell-gonadal tumors among the pediatric population in Turkey and its importance through the eye of gynecologist

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Objective: Childhood cancers constitute a major part of childhood diseases and are an important cause of mortality. Germ cell and gonadal tumors are among the top ten cancers in both boys and girls during childhood. Furthermore, the most common locations of germ cell tumors in the female population under the age of 20 are the ovaries. And germ cell tumors are the most common type of ovarian cancer, in these population. The purpose of this study was to explore the incidence trends of childhood germ cell and gonadal tumors in Turkey and to compare them with those worldwide. And also emphasizes the importance of the approach to the treatment of this cancer in girls. **Methods:** This study is based on data from the Turkish National Cancer Statistics Reports and the International Incidence of 10 Childhood Cancer (IICC) collaborative Project. **Results:** The age specific incidence rates (ASR) of germ cell tumors is 5 per million in Turkey and 4,9 per million across the world. The percentage of germ cell tumors among all childhood cancers in Turkey is 2%-4% in boys and 3,2%-5% in girls. **Conclusion:** Although germ cell and gonadal tumors are among the top ten cancers observed in childhood, their incidence is low. The survival rates of these cancers are very high if they are diagnosed early and accurately. Thus, knowledge about the trends of these cancers will increase the awareness and success in the diagnosis and treatment of germ cell and gonadal tumors.

Keywords

Germ cell-gonadal tumors; Girls; Childhood; Turkey

1. Introduction

In contrast to the adult population, overall, childhood cancers have a much lower incidence, although they constitute an important part of childhood mortality. Cancer research is carried out by the International Agency for Research on Cancer (IARC) within the World Health Organization (WHO). The IARC publishes world cancer incidence and mortality data via the GLOBOCAN database. According to the latest GLOBOCAN report published in 2018, the most common cancer in the world is lung cancer [1]. Data about pediatric cancers can be obtained from the International Incidence of Childhood Cancer (IICC) reports conducted by the IACR. The childhood cancer incidence data of 62 different coun-

tries, including Turkey, from 2001 to 2010, is available the most recent IICC-3 report published in 2017 [2].

IICC is based on the ICD-0-2 morphology and topography codes and it is division into 12 major diagnostic groups [3]. Germ cell-gonadal tumors (GCTs) arising in the gonads (derived from sex stromal or epithelial cells) or in their embryonal precursors, the germ cells. Germ-cell tumors are divided into 3 diagnostic subgroups according to their topographical location these are intracranial and intra spinal germ cell tumors; malignant germ-cell tumors of the ovary or testis (gonadal germ cell tumors); and unspecified non-gonadal germ cell tumors [3].

GCTs are among the top ten most common cancers in childhood. The most common locations of GCTs in the female population under the age of 20 are the ovaries and in the male population the testis. On the other hand, the most frequently observed gynecological cancer in childhood is ovarian cancer with a rate of 1% among all childhood cancers [4]. Among the various subtypes of ovarian cancers, those that arise from the germ cells are the most frequent in children [5, 6].

Unprecedented gains have been made in the cure rates for childhood cancer during the recent years [7]. Although more than 80% of children with cancer who are treated with modern multidisciplinary treatments in developed countries are cured, it's hard to say the same success for low- and middle-income countries [8]. Moreover, the disease burden is not fully known because of the lack of population-based cancer registries in low income countries [8].

The successful treatment of childhood cancer especially germ cell-gonadal tumors can be associated with impaired gonadal function in adulthood. Preservation of fertility before treatment must be considered in all young patient for prevention of subfertility [9]. When the GCTs and gonadal tumors treated correctly by professional and experienced health professionals with fertility sparing approaches, their prognosis will be very favorable. Rare occurrence of this disease results in lack of awareness of physicians and health

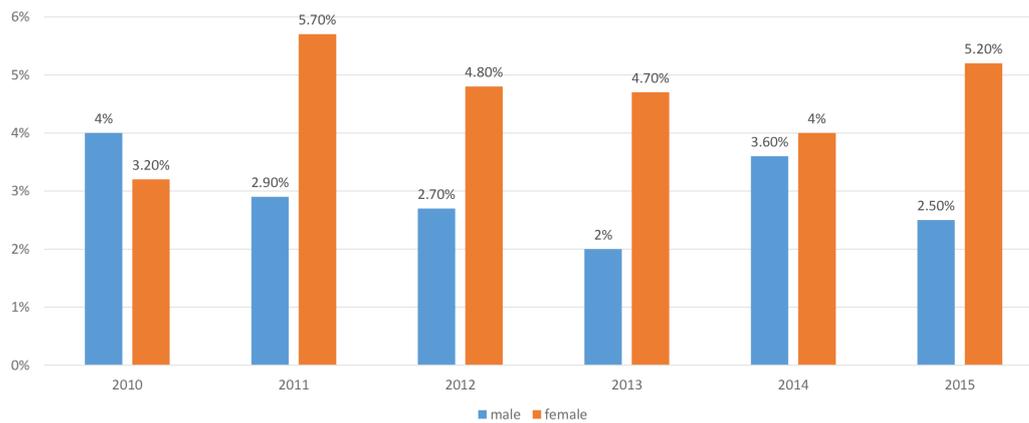


Fig. 1. Distribution of the rates of germ cell tumours in children based on the years and sex in Turkey (2010-2015).

policy makers. The aim of this study was to explore the incidence trend of childhood GCTs in Turkey and to compare them with those worldwide. And it also emphasizes the importance of the appropriate approach to the treatment of girls with GCTs and preserving their fertility.

2. Material and methods

Turkish childhood cancer incidence data were obtained from the National Cancer Statistics Report of the Cancer Control Department at the Turkish Ministry of Health [10]. This report constitutes from active cancer control centers' data which were verified according to the international guidelines and rules of the WHO and checked for completeness, timeliness, and validity by various programs.

The IARC is the leading cancer research organization in the scope of the WHO and publishes available data on worldwide childhood cancer in the form of IICC reports in collaboration with the IACR. ICC-3, the latest volume of the IICC report, was published in 2017 and includes data on the worldwide incidence and age-standardized rates (ASRs) of pediatric cancers from 2001 to 2010, including those from Turkey [2].

Childhood malignancies are defined according to The International Classification of Childhood Cancer (ICCC) is based on the ICD-0-2 morphology and topography codes.

In our report, the boy and girl incidence of germ cell tumors over the years is presented and age is categorized by the groups 0 to 4, 5 to 9, 10 to 14.

This article was prepared in accordance with research and publication ethics.

3. Results

According to the IICC-3 report, the most common cancer in both sexes in the 0-14 age group, worldwide, is leukemia. In most regions of the world, this is followed by central nervous system (CNS) cancers and lymphoma. GCTs are rare, especially in the under the age of 14 and its rate 3.6% in worldwide.

The ASR of the GCTs are 4.9 per million worldwide, but may vary within the different regions (Table 1). This rate was

reported as 5.6 per million for Turkey. The ASRs of the ten most common childhood cancers in the world according to the IICC-3 report are shown in Table 2.

Similar to that reported worldwide, the most frequent cancers in the 0-14 age group in Turkey, according to the Turkish National Cancer Statistics Report, are leukemia, CNS cancers, and lymphomas.

GCTs are among the top ten cancers in both boys and girls. Between 2010 and 2015, the percentage of pediatric germ cell cancers among all childhood cancers in the 0-14 age group varies between 2% and 4% in boys and 3% and 5.7% in girls (Fig. 1).

CNS, gonadal, and other extra gonadal GCTs, gonadal carcinoma, and unspecified gonadal tumors constitute the GCT family. As a subgroup, the ASR of gonadal GCTs is 2.8, and that of other extra gonadal GCTs is 1.8 per million. In addition, the ASR of GCT is 6.3; the ASR of gonadal GCT is 2.8 per million in 0-14 age girls is declared. In boys, the ASR of GCT is 5; gonadal germ cell tumor incidence is 2.9 per million in the same age group.

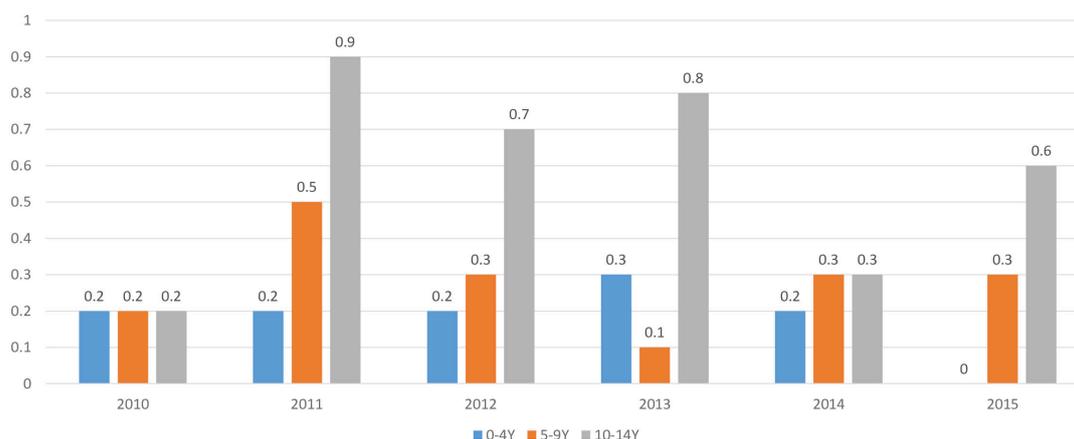
In the IICC-3 report, there is no detailed data on ovarian cancer in childhood. However, the Turkish National Cancer Statistics Report also reveals ovarian cancer is the most common gynecological cancer in the 0-14 age group in Turkey. The incidence of childhood ovarian cancer between 2010 and 2015 varies from 0.6 to 1.6 per 100,000 and no significant difference in the incidence of this cancer has been observed over the years (Fig. 2).

4. Discussion

Despite the low incidence of all childhood cancers, they are an important cause of death in children. According to the GLOBOCAN 2018 database, the ASR of all cancers is 218.6 per 100,000 in males and 182.6 per 100,000 in females worldwide [1]. On the other hand, the ASR of all cancers in the 0-14 age group is 140.6 per million [2]. More importantly, the incidence of childhood cancers is increasing in both low and high income countries worldwide [2].

Table 1. Age Specific Incidence Rates per Million of germ cell tumors in children aged 0-14 years.

	Male (incidence per million)	Female (incidence per million)	Total (incidence per million)
Turkey	5	6.3	5.6
France	4.2	5.5	4.8
Italy	5.2	5.7	5.4
Scotland	3.9	4	4
China	8.9	7.7	8.3
Japan	8.7	8.5	8.6
Egypt	2.2	3.6	2.9
Canada	5	5.6	5.3
USA	4.9	6.1	5.5

**Fig. 2. The incidence of germ cell tumours according to the years and age groups in Turkey (2010-2015).**

Although in childhood, the incidence of GCTs requires attention of physicians, GCTs predominate in girl population in 0-14 age group children [11]. In Turkey, the incidence of GCTs in girls is higher than that in boys. Higher GCTs incidence rates have been reported in boys compared to girls in Japan and China [2]. Katanoda *et al.* reported that the incidence rate of testicular GCT started to increase in the late 10s and surpassed that of ovarian GCTs at the ages of 20 and 30 in Japan [12]. The low incidence rates of GCTs in Africa may be attributed to insufficient cancer registration in Africa.

The GCTs in early childhood and in older children were histologically distinct and occurred at different sites. In children under 1 year of age, tumors are most common in the pelvis in girls and in the testicles in boys, while children between the ages of 10-14 are most frequently detected in the ovary in girls and in the CNS in boys [11]. On the other hand, the numbers of gonadal germ cell tumors in boys and girls are not different from each other [13]. However, the age groups they are seen are different from each other. While more than 80% of cases in boys occurred before the age of 5 years, approximately three-quarters of gonadal germ cell tumors in girls occur after the age of 10 years [13].

The cancer registry is the starting point for the fight against cancer. The official cancer registry in Turkey was started in 1992. Cancer statistics data are published annually in the form of national cancer statistics reports [10]. While

this report can demonstrate cancer incidences by sex and age groups, it does not include cancer survival data. On the other hand, data on cancer survival statistics are not available in the IICC report. In a recent study, the childhood cancer surveillance data was not directly reported, but estimates of global childhood cancer survival using IICC-3 data were provided [14]. According to this report, the global 5-year net childhood cancer survival is currently reported as 37.4%, but can vary significantly by region and country [9]. Moreover, according to this report, the global survival rates of pediatric GCTs range from 20%-48% with gonadal GCTs having the highest rate (47.8%) and gonadal carcinomas presenting with the lowest rate (19%). The highest survival rates were observed in Europe and North America; the survival rates of GCTs in Africa, Asia, Europe, Latin America, North America and Oceania were 13,4%, 44,9%, 86,2%, 65,3%, 94%, and 68,4%, respectively [14]. In another report published by Kaatsch *et al.*, the 5-year survival probability for all GCTs is 92%, with the best survival probability was observed for gonadal GCTs [11]. Furthermore, it was stated that the 5-year survival rate of all the GCTs increased over the years.

Ovarian tumors constitute the most important group of gynecological tumors that occur in children and adolescents. However, the number of cases of childhood ovarian cancers across the world is limited. In a recent review, the number of children with ovarian cancer was reported to be 885 and

Table 2. Age-standardized incidence of the top ten tumors in children aged 0-14 years in the world.

Cancers	Age Specific Incidence Rates per Million
Leukemia	46.4
Central nervous system cancers tumors	28.2
Lymphomas	15.2
Sympathetic nervous system	10.4
Soft Tissue Sarcomas	8.9
Renal Tumors	8.2
Bone Tumors	5.7
Germ Cell and gonadal tumors	4.9
Epithelial tumors and melanoma	4.6
Retinoblastoma	4.5

612 of them presented with GCTs [15]. In the same study, 31 patients with GCTs were identified in Belgium between 2004 and 2013, and most of them belonged to the 10-14 age group. In another study, 93% of the cases of childhood ovarian cancer were GCTs and the median age of the study sample was 13 years [16]. In Turkey, the ASR of ovarian cancer ranges from 0.6 to 1.6 per 100.000, which is consistent with the literature, and this incidence appears to be higher in the 10-14 age group.

5. Conclusions

In conclusion, this is the first report on the trends of childhood GCTs and ovarian cancer in Turkey. Pediatric GCTs generally have a good prognosis. However, data from regions with insufficient cancer registration cannot be evaluated properly. Due to the growing importance of cancer as a health problem for developing countries, the development of national cancer control plans should be encouraged. As cancer registry develops, communities can determine their priorities and country strategies in cancer prevention and care services, and they can follow their success in cancer control activities.

In addition, it is necessary to add survival data to studies examining childhood cancer incidence data for treatment strategies and follow-up plans for these cancers.

Author contributions

I.A.K and M.G.: Design the study; I.A.K and M.G.: analysis or interpretation; I.A.K.: Literature search; I.A.K and M.G.: writing manuscript; M.G.: critical review.

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Conflict of interest

The authors have no competing interests to declare.

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