Epidemiology of Childhood Cancer in Northeast of Iran

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Abstract
Background: Malignant neoplasms remain the second leading cause of death in children after accidents. The aim of this study was to assess the epidemiology of childhood cancer in children admitted to Dr sheikh hospital, Iran.

Materials and Methods: This descriptive cross-sectional study had been done in Dr Sheikh Hospital in Mashhad University of medical science on 1764 children younger than 14 years old from 2006 up to 2014 with cancer that has been pathologically confirmed. All information about the age, sex, type of cancers, and the residence of patients were collected and recorded from their medical records.

Results: regarding gender, 1055 of cases were male and 709 female. The mean age of patients was 5.8±4.2 years old while 30% were in age group of 3-6 years. Results showed that leukemia (56.4%), Lymphomas (10.3%), renal tumor (9.3%), malignant bone tumor (4.4%), and CNS tumor (4.1%) were the most prevalent malignancies in children admitted to Dr Sheikh hospital in Mashhad, Iran. The most common form of leukemia was ALL (86.9%). during the course of the study, the lowest and highest age standardized incidence rate was 114 (2006) and 142 (2014) cases out of each 1000,000 person, respectively.

Conclusion: Distribution of childhood cancer in terms of year revealed the increase of malignant tumor prevalence about 2.5% from 2006 to 2014. Incidence of childhood cancers in Dr Sheikh hospital in Northeast of Iran was similar to neighboring province and other countries.

Key words: Cancer, Child, Epidemiology, neoplasm

Introduction
Cancer is the leading cause of disease-related death among children aged between 0 to 14 years old. According to estimations, 10,380 new cases of pediatric cancer in children aged between 0 to 14 years old would be diagnosed in 2015, with an estimated 1250 deaths(1). more than 8,500 children younger than 15 years are diagnosed with cancer each year in the United states(2). Cancer incidence allocated the third rank of death cause to itself in Iran after coronary heart disease and accidents. World Health Organization (WHO) also estimated the incidence rate of childhood cancer as about 100 per million children(3). Even rare, childhood cancers are representing between 0.5% and 4.6% of all cancers (4). The population of Iran is about 70 million while 29% are children. A literature review on published articles was conducted using different search demonstrated that the incidence rate of childhood cancer in Iran was 48 to 112 and 51 to 144 per million among girls and boys in multi geographical settings, respectively(5).

Overall, similar to other regions of Iran(3, 5, 6) and other developing countries like India(7), Mexico city(8), and Japan(9), acute lymphoid leukemia is the first most common malignancy. Fathi et al., reported
the epidemiology of childhood cancer in northwestern Iran and maintained that Leukemia (54.2%), CNS (12.1%), and lymphoma (8.4%) were the most common cancer in children, respectively (3). Jafroodi in Rasht showed that the most common cancers in children were leukemia (54.6%) (10). The results of Golestan study during 2004-2006 depicted that leukemia, CNS tumors, and lymphomas were the first three childhood cancers (11). The results of Fars study showed that leukemia (47.8%), CNS tumors (9.5%), lymphomas (9.3%), malignant bone tumor (7.1%), and renal tumor (3.3%) were first five childhood cancers (12). The result of Sari study showed that leukemia (30.5%), lymphoma (16.4%) carcinoma, and melanoma (14.5%), soft tissue sarcoma (9.5%), neuroblastoma (6.5%), and CNS tumors (4.7%) were most common in childhood cancers (13). In German, Childhood Cancer Registry (GCCR) during 1980-2005 was conducted on Turkish migrant children and held that the three top cancers were leukemia, Hodgkin’s disease and Non Hodgkin lymphoma (14). Another study in Germany showed that leukemia (34%), brain tumors (23%), and lymphomas (12%), represent the largest diagnostic groups among the children under 15-year-olds (15). Holmes declared that the most commonly diagnosed malignancies are acute lymphoblastic leukemia (ALL), central nervous system (CNS)/brain, and renal cancer (1). Reports from Latin America and Asian countries show that CNS tumor were more common than lymphoma (2, 16). A ten years study (1990-1999) in India listed the common malignant neoplasm in children in descending order of frequency as follows: ALL (39.2%), retinoblastoma (19.2%), lymphoma (10.8%), and tumor wilms (10%). Brain tumors were not found due to non-availability of neurosurgical unit in this institution. Frequency of neuroblastoma was very low, only 2(1.6%) out of a total of 120 (17).

Race, ethnicity, sex, age group, socioeconomic status, and geographic locale are common indicators of disparities in childhood cancer. The etiology of childhood cancers is largely unknown. Although genetic factors play an important role in the development of childhood cancers, the role of environmental factors, maternal use of oral contraceptives, living in proximity to high voltage power lines, in-utero ionizing radiation exposure, pesticide exposure in fathers, paternal occupation and parental smoking are also substantial (18). In a case control study about the relationship between socioeconomic status and childhood leukemia, a significant difference was found in terms of parental education level and income status between two groups (19). So far, few environmental risk factors, such as exposure to air pollutants and radiation have been suggested to be associated with the development of childhood cancers. However, these risk factors describe only a small proportion of childhood cancers. Nevertheless, environmental risk factors play an important role in the incidences of childhood cancers (20).

Clinical epidemiologic studies’ finding of regarding pediatric malignancies are challenging and limited. The incidences of these malignancies are varied throughout the world with regard to age, gender, ethnicity, socioeconomic status, and geography (13). Childhood cancer is not a single disease and has various types and pathogenic causes with various histopathology features and can occur in different parts of human body (21). Leukemia (incidence rate = 8 to 62/million), central nervous system tumors (CNS) (3 to 22), and Lymphoma (3 to 23) are the prevalent cancers in childhood (5).

The estimation of cancer incidence sometimes result in difficulties and complexities due to the unavailability of
accurate population size data to serve as the denominator for cancer diagnosed in various settings. Due to limitation in population data, there are few studies that have estimated incidence or cumulative incidence in childhood cancer. Controlling the burden of cancer should be done by collecting data about frequency, type and places of cancer incidence. Few epidemiologic studies on cancer have been carried out in Iran. The aim of this study was to assess the epidemiology of childhood cancer in children who admitted to Dr sheikh hospital in Mashhad, northeast of Iran. The result of this study can provide beneficial information to plan new childhood cancer management.

Materials and Methods
This descriptive cross-sectional study had been done in Dr sheikh Hospital in Mashhad, Iran on 1764 cancer children during 2006-2014. All the participants were younger than 14 years old at the time of diagnosis (during 2006-2014). Their disease were pathologically confirmed. All cancer cases aged between 0-14 years. For classification of the lesions, the tenth edition of International Classification of Childhood Cancer (ICCC-10) coding system was use; it applied the rules, nomenclature and codes (morphology, topography, and behavior) of the tenth edition Classification of Diseases for Oncology (ICD-O-10). All information about the age, sex, type of cancers, and residence of patients were collected from their medical records. Frequency distribution of childhood cancers was evaluated and the incidence rates were calculated per 100,000 people a year. 1764 forms were completed and the data were analyzed by SPSS (version21).

Results
In this study which was conducted from 2006 to 2014, 1764 cancer cases were recruited. Regarding sex, 1055 (60%) of cases were male and rest of them were female by sex ratio 1.5 to 1. The mean age of patients was 5.8± 4.2 while 526 cases (30%) were in age group of 3-6 years. Results showed that leukemia (56.4%), lymphomas (10.3%), renal tumor (9.3%), malignant bone tumor (4.4%), and CNS tumor (4.1%) were the most prevalent malignancies in Northeast Iran (Table I). From leukemia cases, 86.9% were acute lymphatic leukemia (ALL). Distribution of childhood cancer by year revealed that from 2006 to 2014, the number of malignant tumor increased about 2.5%. Over these nine years period, the lowest and highest age standardized incidence rate was 11.4 (year 2006) and 14.2 (year 2014) cases per every 100,000 person, respectively (Table II).
### Table 1: Distribution of Childhood Cancer by Gender, site and age group

<table>
<thead>
<tr>
<th>Site</th>
<th>Age group</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1m</td>
<td>1m-1y</td>
</tr>
<tr>
<td>Leukemia (ALL 86.9%. AML 13.1%)</td>
<td>2(0.1%)</td>
<td>52(3%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0(0%)</td>
<td>2(0.1%)</td>
</tr>
<tr>
<td>Renal tumor</td>
<td>2(0.1%)</td>
<td>31(1.75%)</td>
</tr>
<tr>
<td>Malignant bone tumor</td>
<td>2(0.1%)</td>
<td>7(0.39%)</td>
</tr>
<tr>
<td>CNS</td>
<td>1(0.05)</td>
<td>6(0.34%)</td>
</tr>
<tr>
<td>Hepatic tumor</td>
<td>2(0.1%)</td>
<td>14(0.79%)</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>1(0.05)</td>
<td>4(0.2%)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>0(0%)</td>
<td>3(0.17%)</td>
</tr>
<tr>
<td>Others</td>
<td>4(0.2%)</td>
<td>30(1.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>14 (0.8)</td>
<td>149 (8.5%)</td>
</tr>
</tbody>
</table>
Discussion

The present study, conducted for the first time in Northeast Iran, revealed childhood cancer pattern according to ICD-10 (International Statistical Classification of diseases And Related Health Problems Tenth Revision). This study provided insight into the distribution of cancer among children who admitted to Dr sheikh hospital in Mashhad, Northeast of Iran. The ratio of male to female was 1.5 to 1. Which was consistent with similar report in Yazd (1.53)(6), Sari (1.24)(13), Rasht (1.41)(10),Fars (1.32)(12), England (1.28), Mexico city (1.1)(8), and United State (1.23%) (1).

The epidemiology of childhood cancer in this study except CNS tumor was similar to another study (3). In Mashhad, the majority of children with CNS tumor were admitted to another hospital. However, Dr Sheikh hospital is the only hospital for the treatment of childhood cancer except CNS tumor.

In this study, most of cases (30%) were in age group of 3-6 years and the least number of participants aged<1 which was compatible with Gilan study. In Gilan, most of cases were in age group 3-4 years which were similar to the current study (10). Hashemi reported that most frequent cancer children are aged between 6to7 years and this epidemiology was rarel observed in children<1 years of age(6). In a study conducted by Fathi, most of cancer cases (30%) were found in age group of 0-4 years(3). Ghasemi reported the highest frequency of cancer in 5-9 years age group and the lowest in 0-4 years (13). In united states, most of cases were in age group of 0-4 years(1).

Distribution of childhood cancer by year reveals that from 2006 to 2014 the frequency of malignant tumor has been increased only 2.5%. Another study in Iran reported increasing trend about 2% per year(13). The overall incidence rate for childhood cancers has increased significantly by almost 33% during the period of 1975 to 2001; although, in more recent years, the rate has been leveling off (2).

Over these nine years period, the lowest and the highest age standardized incidence rate was 114 (year 2006) and 142 (year 2014) cases per every 1000,000 person, respectively.

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency</th>
<th>Incidence per 1000,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>177</td>
<td>10</td>
</tr>
<tr>
<td>2007</td>
<td>178</td>
<td>10.1</td>
</tr>
<tr>
<td>2008</td>
<td>185</td>
<td>10.5</td>
</tr>
<tr>
<td>2009</td>
<td>179</td>
<td>10.2</td>
</tr>
<tr>
<td>2010</td>
<td>196</td>
<td>11.1</td>
</tr>
<tr>
<td>2011</td>
<td>193</td>
<td>11</td>
</tr>
<tr>
<td>2012</td>
<td>218</td>
<td>12.3</td>
</tr>
<tr>
<td>2013</td>
<td>218</td>
<td>12.3</td>
</tr>
<tr>
<td>2014</td>
<td>220</td>
<td>12.5</td>
</tr>
<tr>
<td>Total</td>
<td>1764</td>
<td>100</td>
</tr>
</tbody>
</table>
The cumulative incidence rate in Northwest Iran was 95.4 patients per one million (3). In Farahmand et al.'s study, the most and least incidence rates were in years of 2006 and 2001 with 235 and 64 per 1000000, respectively (12). The age-standardized incidence rates for childhood cancer in Golestan province of Iran were 119.8 and 78.3 per 1000000 person-years in male and female children, respectively (11). In Switzerland, the crude incidence of childhood cancer in children aged <14 years was 135 per 1000000 (16). Incidence of childhood cancers in the Northeast Iran was similar to neighboring provinces and countries.

**Conclusion**

This is the first study which investigated the distribution of pediatric cancers in Northeast Iran. Results showed that leukemia, lymphomas, renal tumor, malignant bone tumor, and CNS tumor were the most prevalent malignancies in Northeast Iran. Distribution of childhood cancer by year revealed that from 2006 to 2014 the number of malignant tumor increased only 2.5%. This result can be due to a low level of awareness regarding cancer among clinicians and the population, inadequate access to health care, lack of diagnostic equipment and incomplete recording of cases. Improvements on various levels (e.g., training more pediatricians about symptoms of childhood and adolescent cancer, availability of diagnostic equipment, good documentation of medical information in hospitals) should be implemented to get a better insight into the size of this ‘health problem’ and to detect cancer earlier, which will subsequently bring about a better outcome for affected children.

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**Conflict of interest**

There is no conflict of authors.

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