



Prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies: A systematic review and meta-analysis

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Abstract

Objective: the aim of this systematic review and meta-analysis was to evaluate the prevalence of central nervous system in Iranian childhood malignancies.

Methods: The present systematic study has applied developed methods that are in line with accurate instruction of PRISMA checklist. Two researchers have separately investigated all studies conducted up to May 2010; the studies had been collected from international databases (PubMed, Google Scholar, and WOS) and national ones (SID and Magiran) without any time limitation in both English and Persian.

Results: As many as five studies conducted on 2851 children were included in the meta-analysis. In asymptomatic children, according to the results of random effects mode, the general prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies was 4.3% in 2851 children (95% CI: 3.5, 5.1; $I^2=56.4\%$).

Conclusion: Given the few number of patients, there is no consistent treatment method for CNS involvement in malignant tumors occurring out of the CNS. Moreover, most of the drugs taken for tumors out of the CNS cannot pass through the blood-brain barrier. When the CNS is involved, it is required to review the initial medical method and adopt a more effective treatment. Thus, determining the involvement prevalence of CNS in children is necessary for finding more effective drugs as well as more efficient medical protocols.

Keywords: Malignancy, children, CNS, Iran

Introduction

Childhood cancers (also known as pediatric cancers) are regarded as the main causes of death in children and teenagers of developed countries; after unintentional injuries, cancer is the second most important cause of death among children (1).

Children account for nearly 20% of all cancer cases in industrial countries (2). Thus, with annual incidence rate of 150 new cases per one million children, children's cancers are relatively uncommon (3-5). However, cancer accounts for 10% of death in children. Moreover, after accidents, cancer is known to be the second cause of death in children (6). For this reason, children's cancer is regarded as the main cause of death in children (7).

The most common childhood cancers include acute lymphoblastic leukemia (ALL), central nervous system tumors, and lymphomas (8). These three cancers account for more than a half of all cancer cases in children. Children's cancers are remarkably different from those of adults in terms of prognosis, histological distribution, and tumor location (9). *Acute lymphoblastic leukemia* (ALL), central nervous system tumors, lymphomas, soft-tissue sarcoma, and bone sarcoma are seen in children and teenagers (10). In contrast, epithelial tumors of organs such as lungs, colon, breast, and prostate are more common in adults. In the age range of under 19 years, one is faced with two peaks at the beginning of childhood and adolescence (11). Although childhood cancers are likely to be seen at any age, special cancers are more possibly seen at specific ages. Over the first year of life, embryonal tumors such as neuroblastoma, Wilms' tumor (also known as nephroblastoma), retinoblastoma, rhabdomyosarcoma, and medulloblastoma are the most common type of cancers that are more possibly congenital (12).

As the incidence and prevalence of cancers vary in different parts of the world and they are affected by numerous cultural and environmental factors, an effective step can be taken towards training the society, prevention, early diagnosis, and disease reduction through identifying the risk factors of children suffering from cancer.

Materials and Methods

The present systematic study has applied developed methods that are in line with accurate instruction of PRISMA checklist. However, only observational studies including letters to the editors, journals, poor quality articles (based on HOY tool), and studies conducted on adult participants were removed from the study. It was attempted to include studies only in English and Persian. All observational studies with any sampling and statistical designs have been included in the present systematic study. Two researchers have separately investigated all studies

conducted up to November 2018; the studies had been collected from international databases (PubMed, Google Scholar, and WOS) and national ones (SID and Magiran) without any time limitation in both English and Persian. The reference list of the existing studies has been also investigated to find more studies in this regard. Special research strategies have been adopted by a health science librarian (an expert on systematic studies) through applying MESH browsing vocabulary as well as free vocabulary based on PRESS standard (16). Moreover, MEDLINE research strategy has been applied for searching other databases as well. The keywords applied in the research strategy include: Central Nervous System ,tumor, Malignancies, children, and Iran that were combined with Boolean operators such as AND, OR, and NOT. Two researchers have separately investigated the titles and abstracts by considering the qualification criteria. After excluding the repetitive studies, the full texts of the studies were investigated based on the qualification criteria and the required information was extracted. For solving the questions on qualifications, extra information was obtained from the authors whenever needed. Moreover, the required data on conditions, sample size, risk of bias, and the measurement of result (prevalence of CNS involvement) were collected as well. The final extracted data were evaluated by using STAT 14.0.

Results

Study selection: In total, as many as 315 studies were selected from the initial research on PubMed, Google Scholar, SID, Magiran, and Web of Science from the beginning to May 1 of 2019. From 285 non-repetitive studies (in terms of title and abstract), as many as 269 studies were excluded in the screening process; their titles were unrelated. From the remaining 16 studies, 5 studies were qualified for having the required criteria. From 11 excluded studies, 2 studies were reviewed, 2 studies were sent to the editor in chief (letter to editor), 3 studies didn't have the full texts, and 4 studies didn't meet the minimum quality and standards required to be included in this study (Figure 1).

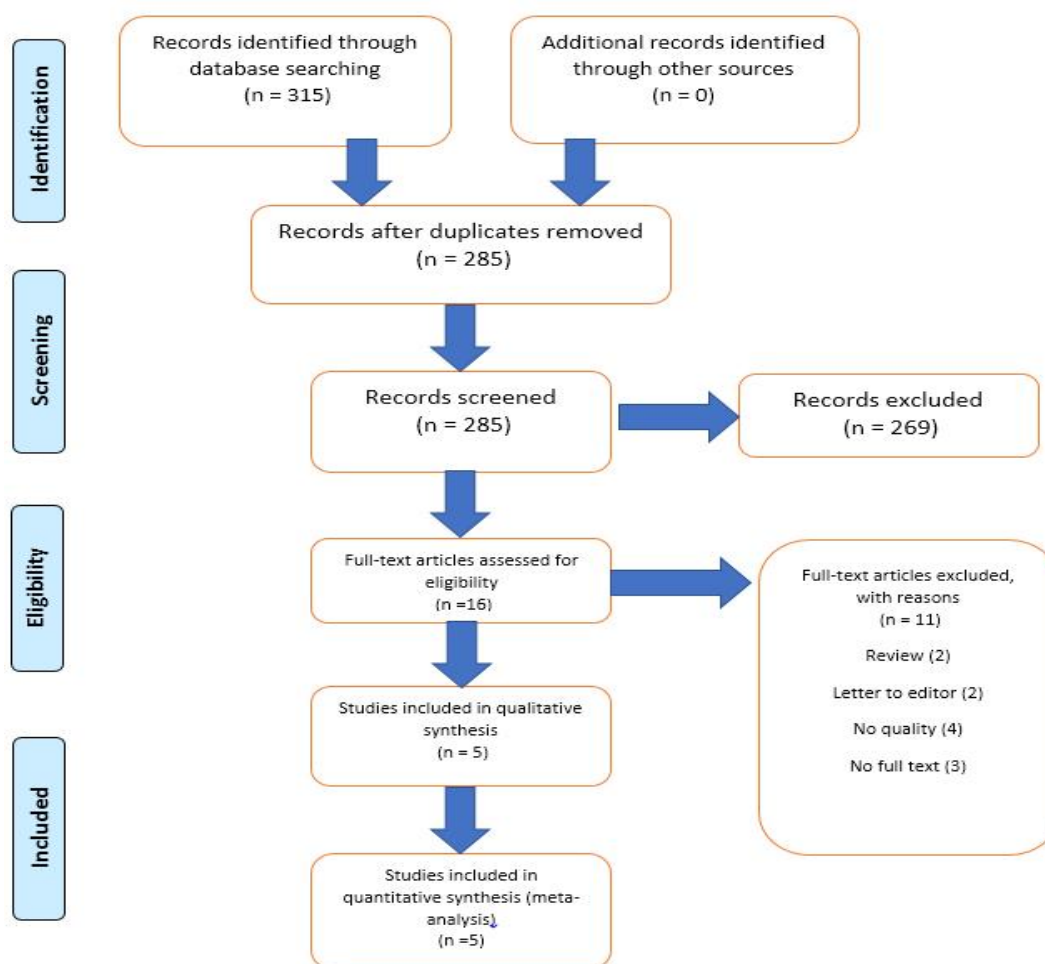


Fig 2. PRISMA flow diagram

Research characteristics:

These 5 studies had been conducted on 2851 Iranian aged <14 years. From these 5 studies, 4 studies have provided cross-sectional data, and one study was a prospective research. Moreover, each of Tehran , Yazd, Isfahan , Gilan and Mashhad provinces accounted for one study. The most common sampling method applied was convenience sampling method (n=4). More than 75% of the studies had low risk of bias. Hospital was the most prevalent place for conducting the studies (n=4).

Prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies

As many as five studies conducted on 2851 children were included in the meta-analysis. In asymptomatic children, according to the results of random effects mode, the general prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies was 4.3% in 2851 children (95% CI: 3.5, 5.1; $I^2=56.4\%$) [Table1].

Table 1: Characteristics of final included studies

Author	Year	City	N	ES	95% conf. Interval		Weight
					Low	Up	
Boroumand ⁽²⁰⁾	2016	Mashhad	1764	0.044	0.035	0.053	73.12
Mehdiabadi ⁽²¹⁾	2005	Tehran	287	0.045	0.021	0.069	11.32
Hashemi ⁽²²⁾	2006	Yazd	106	0.094	0.039	0.149	2.10
Beheshti ⁽²⁴⁾	2002	Isfahan	542	0.012	-0.015	0.039	8.85
Jafrودي ⁽²⁵⁾	2008	Gilan	152	0.059	0.022	0.096	4.62
Pooled ES	-----	-----	2851	0.043	0.035	0.051	100

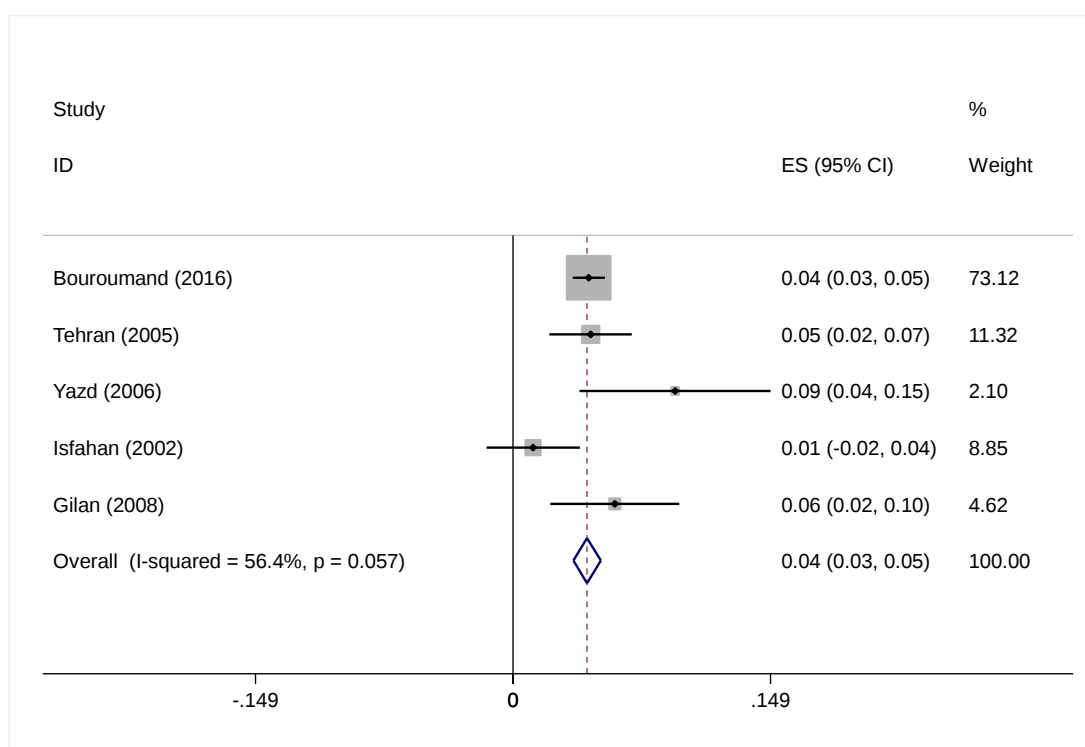


Fig 2 .: Prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the% value and the length of the lines showing the 95% confidence interval in each study. The oval sign shows Prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies

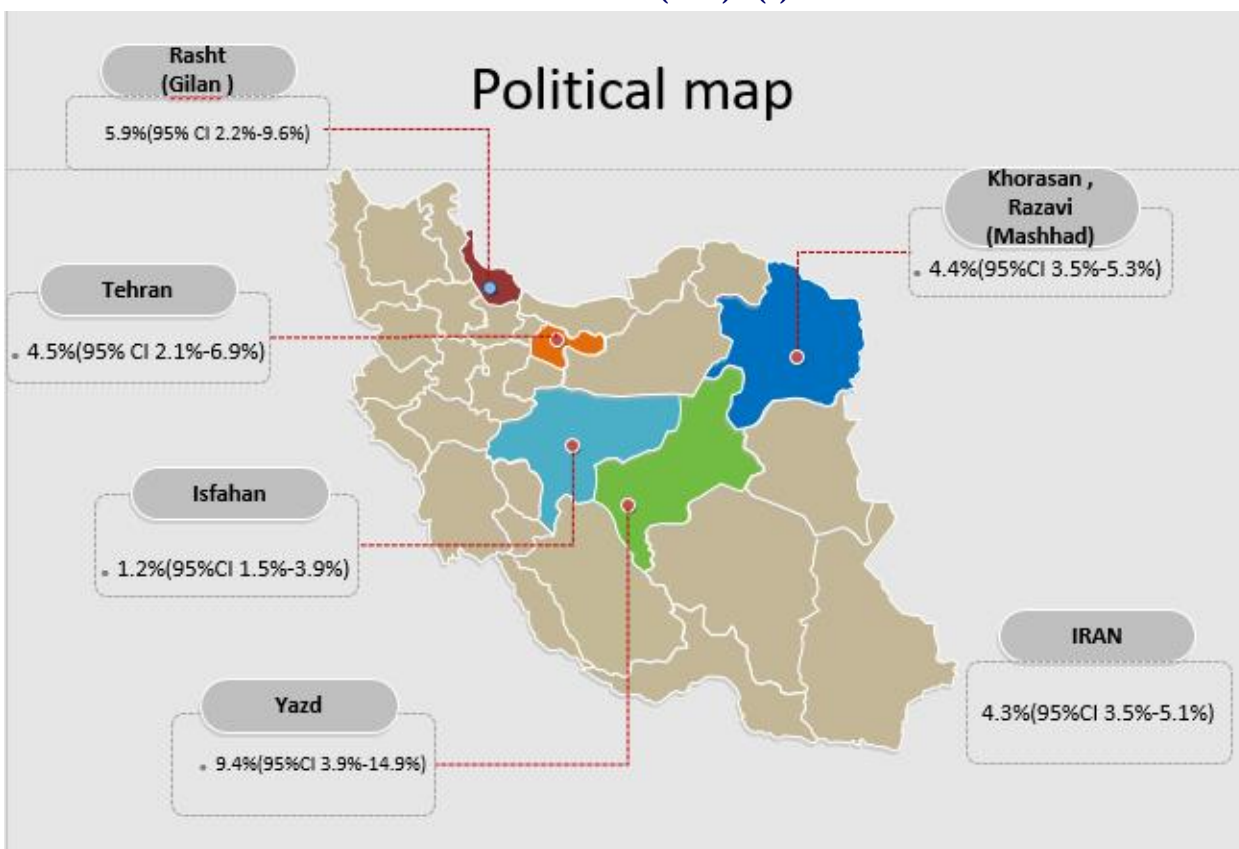


Fig 3 .Prevalence of Central Nervous System Involvement in Iranian children (according to the frequency in children of each province)

Discussion

As many as five studies conducted on 2851 children were included in the meta-analysis. In asymptomatic children, according to the results of random effects mode, the general prevalence of Central Nervous System Involvement in Iranian Childhood Malignancies was 4.3% in 2851 children (95% CI: 3.5, 5.1; $I^2=56.4\%$). Cancer is one of the most important causes of death on adults. After cardiovascular diseases, cancer is the second most important cause of death. In children, the significance of this disease depends on its early diagnosis; children's cancers can be treated if they are diagnosed early.

In comparison to girls, childhood cancers are more frequently seen in boys. Moreover, children's cancers are different from those of adults in terms of tumor types as well as tumor locations (13). There are two age maximums for the incidence of childhood cancers: early childhood and adolescence. In the early years of

life, embryonal tumors such as neuroblastoma, Wilms' tumor (also known as nephroblastoma), *retinoblastoma*, rhabdomyosarcoma, hepatoblastoma, and *medulloblastoma* are the most common tumors. In the age range of 2-5 years, in addition to embryonal tumors, acute leukemia, non-Hodgkin lymphomas, and glioma have the incidence rate (14). At the age of puberty, bone cancers, Hodgkin lymphoma, testicular cancer, and ovarian cancer have the highest incidence rate (15). Given the few number of patients, there is no consistent treatment method for CNS involvement in malignant tumors occurring out of the CNS (16). Moreover, most of the drugs taken for tumors out of the CNS cannot pass through the blood-brain barrier (17). When the CNS is involved, it is required to review the initial medical method and adopt a more effective treatment. Thus, determining the involvement prevalence of CNS in children is necessary for finding more effective drugs as well as more efficient medical protocols (18-20).

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