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Incidence of childhood cancer in Costa Rica, 2000–2014: An international perspective

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ABSTRACT

Background: Estimating childhood cancer incidence globally is hampered by a lack of reliable data from low- and middle-income countries. Costa Rica is one of the few middle-income countries (MIC) with a long-term high quality nationwide population-based cancer registry.

Methods: Data on incident cancers in children aged under 15 years reported to the Costa Rica National Cancer Registry between 2000 and 2014 were analyzed by diagnostic group, age, sex, and geographical region and compared with incidence data for Hispanic and Non-Hispanic White (NHW) children in California, USA.

Results: During the 15-year period, 2396 cases of childhood cancer were reported in Costa Rica, resulting in an overall age-standardized incidence rate (ASR) of 140/million. Most frequent cancer types were leukemias (40.5%), malignant central nervous system (CNS) tumors (13.9%), and lymphomas (12.7%). The observed ASR of lymphoid leukemia (46.9/million) ranked high globally. Low rates were found for most solid tumors including malignant CNS tumors, sympathetic nervous system tumors, and soft tissue sarcomas. There was almost no change in incidence rates over time, while geographical variations were observed within Costa Rica. The overall cancer rate in Costa Rica was lower compared to NHW (176.1/million) and Hispanic (161.7/million) children in California.

Conclusion: Based on the longstanding registration system, the childhood cancer incidence rates were similar to those observed in other Latin American countries. While a degree of under-ascertainment of cases cannot be excluded, the markedly high leukemia rates, in particular of the lymphoid sub-type deserves further study in this population.

1. Introduction

Little is known about the aetiology of childhood cancers. Many studies targeted lifestyle factors or environmental pollutants as possible risk factors but with inconsistent results [1,2]. To date, a few genetic conditions, exposure to high-dose ionizing radiation and prior chemotherapy, and high or low birth weight have been confirmed as risk factors [1], but only explain a small percentage (< 10%) of all cases [1,2]. Early age at diagnosis indicates that childhood cancer might originate *in utero* and that prenatal, including preconception, factors or early-life environmental exposures may be important determinants [3,4].

Population-based cancer registries around the world report incidence rates in children under the age of 15 years that vary between less than 70 to more than 200/million per year [5] for all cancers. Describing incidence patterns and identifying geographical differences, especially in genetically-related populations may provide useful indications for possible aetiological associations and observed geographical incidence differences have been used to support several hypotheses of the association between exposures related to modern

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lifestyle and the risk of childhood cancer, particularly leukemia [3].

However, estimating childhood cancer incidence globally is hampered by a lack of reliable data, especially marked in low- and middle-income countries (LMIC), including in Latin American countries. Incidence patterns are relatively consistent and well described for economically developed countries [6], with recent age-standardised incidence rates of 168, 176, and 155/million children being reported for Germany [7], US Non-Hispanic Whites (NHW) [5], and Australia [5], respectively. In contrast, childhood cancer rates of 46, 111, and 129/million have been reported for South Africa [8], Thailand [5], and Argentina [9], respectively, with a variation in the distribution of cancer types across these middle-income countries (MIC) and in comparison to high-income countries (HIC). Reported incidence rates for leukemia, the most common childhood cancer type in HICs [5], and for cancer in infants are considerably lower in many LMICs compared to HICs [5,10]. Simultaneously, some Latin American cancer registries including Costa Rica, consistently report very high incidence rates of leukemia [5].

Geographical variations in incidence rates may indeed indicate differences in genetic or environmental exposures that affect the risk of childhood cancers (or certain types of childhood cancer). However, evidence from Brazil [11], India [12], and South Africa [8] suggest that incidence differences across countries may also reflect under-diagnosis and/or under-reporting of cases in LMICs.

Costa Rica is an upper-middle income country [13] with a nationwide population-based cancer registry that has provided internationally comparable data for more than four decades and is also home to an ethnically homogenous population (i.e., most Costa Ricans are considered mestizos) [14]. Moreover, Costa Rica has a national public health care system (funded by employer, employee, and government) that provides free access to primary, secondary, and tertiary public health care for children until the age of 18 years [15]. This health care system gives every child with cancer the possibility to get diagnosed and treated for free. The National Children's Hospital situated in the capital San Jose is the only public specialized pediatric oncology treatment center in Costa Rica (see Fig. 1). In this report, we provide the first comprehensive description and interpretation of the incidence of childhood cancers diagnosed between 2000 and 2014 in Costa Rica by cancer type, age, sex, and place of residence. Furthermore, we discuss our findings in a global perspective and compare our results with data for Hispanics and NHW children in California, USA. Comparing the incidence of Costa Rica with the genetically-related population of Hispanics provides the basis for considering the potential impact of differences in diagnosis, reporting, and potential environmental risk factors, while comparison with NHW may suggest differences in genetic susceptibility.

2. Material and methods

2.1. Costa Rica National Cancer Registry

The Costa Rica National Cancer Registry (RNT, for its acronym in Spanish) was founded in 1976 and reached nationwide coverage in 1980 [16]. Reporting each diagnosed cancer case to the RNT is mandatory for all public and private hospitals and clinics, health care units, and clinical and pathology laboratories in Costa Rica. In addition, the RNT reviews all death certificates at the Central Bureau of Statistics and Census on a yearly basis. Cases notified from death certificates are traced back to medical records and if their diagnosis is supported clinically or microscopically, the registry record is updated; otherwise it stays death certified only (DCO). The DCO cases represented 1.7% of the childhood cancer cases diagnosed between 2000 and 2014, while 91.5% of diagnoses were confirmed microscopically (histology or cytology). Diagnoses are coded based on primary organ site and morphological type according to the International Classification of Diseases for Oncology, third edition (ICD-O-3) [17].The RNT registers only tumors of malignant behaviour (or in situ), not benign tumors. Each multiple primary cancer is recorded as an additional case.

2.2. California Cancer Registry

The California Cancer Registry (CCR) is a state-wide population-based registry that collects information on incident cancers diagnosed among California residents since 1988. State law requires any hospital or other health care facility that diagnoses or treats cancer patients to report the cancer case to the registry. The CCR collects information on all primary malignant and *in situ* cancers (except certain carcinomas of the skin) and benign and borderline tumors of the brain and central nervous system [18]. The CCR follows the National Cancer Institute Surveillance Epidemiology and End Results (SEER) Program's multiple primary rules to distinguish a single primary from multiple primary tumors at the time of diagnosis [19]. Cancers in the CCR are classified according to ICD-O-3. Each year, the CCR performs a record linkage with a file of all deaths in the state. If a cancer death does not link to an existing cancer registry case, and no additional information on the cancer is found through follow-back to medical facilities, the case is added to the registry and designated as a DCO case. Less than one percent (0.03%) of childhood cancer cases diagnosed in California between 2000 and 2014 were DCO cases, whereas 92.7% were microscopically confirmed.

Demographic information for cases in the CCR, including a patient's ethnicity and race, come mainly from medical records. This information may be based on self-report by the patient or their family or on assumptions made by medical personnel. The CCR uses various methods to enhance the identification of a patient's ethnicity and race and may infer this information based on birthplace, maiden name, surname, or parents' race [20]. In the CCR data Hispanics may be of any race, however 97.9% of cases identified as Hispanic are racially White.

The CCR was chosen as a reference registry because of the similarities in the genetic make-up between Costa Rican [21] and Californian Hispanic children [22].

2.3. Case definition

All malignant neoplasms diagnosed in patients younger than 15 years of age during the period 2000–2014 were obtained from the RNT and recoded into 12 major diagnostic groups and 47 subgroups according to the International Classification of Childhood Cancer 3rd edition (ICCC-3) [23]. Only one cancer case registered by the RNT during the period of interest had a combination of morphology and topography codes that did not correspond to a specific ICCC-3 group and was retained in the analyses as unclassified.

2.4. Definition of geographical regions in Costa Rica

The territory of Costa Rica is divided into seven provinces which are subdivided into 82 counties (also called cantons), and these are further subdivided into districts. Districts have also been grouped into six geographical regions (i.e., Central, Chorotega, Pacífico Central, Brunca, Huetar Atlántica, and Huetar Norte) that were established by the Costa Rican Ministry of Planning and Economic Policy (MIDEPLAN) in 1978 (Fig. 1). These geographical regions were defined based on social, political, and economic characteristics such as population homogeneity, availability of natural resources, and predominant productive activities [24], and are commonly used for periodical statistical reports, including population counts.

Each MIDEPLAN region is comprised of multiple districts that do not necessarily belong to the same county. This is a challenge when classifying the residences of the cases reported to the RNT into MIDEPLAN regions because counties are commonly used to record these residences in the registry and access to the exact addresses is not permitted. There are three counties (i.e., Alajuela, San Ramón, and Grecia)