Cancer Epidemiology 52 (2018) 83–90

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Temporal and geospatial trends of pediatric cancer incidence in Nebraska over a 24-year period

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ARTICLE INFO

Keywords:
Pediatric cancer
Epidemiology
Rural

ABSTRACT

Background: Data from the Surveillance, Epidemiology, and End Results (SEER) revealed that the incidence of pediatric cancer in Nebraska exceeded the national average during 2009–2013. Further investigation could help understand these patterns.

Methods: This retrospective cohort study investigated pediatric cancer (0–19 years old) age adjusted incidence rates (AAR) in Nebraska using the Nebraska Cancer Registry. SEER AARs were also calculated as a proxy for pediatric cancer incidence in the United States (1990–2013) and compared to the Nebraska data. Geographic Information System (GIS) mapping was also used to display the spatial distribution of cancer in Nebraska at the county level. Finally, location–allocation analysis (LAA) was performed to identify a site for the placement of a medical center to best accommodate rural pediatric cancer cases.

Results: The AAR of pediatric cancers was 173.3 per 1,000,000 in Nebraska compared to 167.1 per 1,000,000 in SEER. The AAR for lymphoma was significantly higher in Nebraska (28.1 vs. 24.6 per 1,000,000; $p = 0.009$). For the 15–19 age group, the AAR for the 3 most common pediatric cancers were higher in Nebraska ($p < 0.05$). Twenty-three counties located > 2 h driving distance to care facilities showed at least a 10% higher incidence than the overall state AAR. GIS mapping identified a second potential treatment site that would alleviate this geographic burden.

Conclusions: Regional differences within Nebraska present a challenge for rural populations. Novel use of GIS mapping to highlight regional differences and identify solutions for access to care issues could be used by similar states.

1. Introduction

Cancer is the leading cause of death from disease among children in the United States [1]. In 2017, it is expected that there will be 10,270 new cases of pediatric tumors in children 0–14 years old [1]. Pediatric cancer represents a spectrum of diseases. A report of pediatric cancer incidence from 62 countries revealed an AAR of 140.6 per million person-years in children 0–14 years old (2001–2010). Leukemia was the most common cancer, followed by CNS tumors and lymphomas [2]. A study in the United States showed that acute lymphoblastic leukemia (ALL) increased during 2001–2008 and was most prevalent in Hispanic populations and Western regions of the US [3]. Furthermore, disparities in pediatric cancer mortality have been suggested in a Tennessee study, which showed that African American children tended to reside in proximity to death clusters in rural areas [4].

The etiologies of pediatric cancers are poorly understood; genetic and environmental factors play key roles [5]. Pediatric cancer patient care remains an imposing challenge to patients and their families since treatment often requires multiple therapeutic techniques (e.g., surgery, chemotherapy, radiation therapy, stem cell transplantation [6]) administered by a team of specialists located in an urban area [7,8]. Consequently, a major public health issue arises for states with a large rural population living a great distance from urban specialized children's cancer care centers [8,9]. The problem is further magnified by the fact that three-quarters of pediatric cancer survivors will require long-term subspecialty management [10]. Therefore, from the time of

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https://doi.org/10.1016/j.canep.2017.12.006
Received 10 August 2017; Received in revised form 12 December 2017; Accepted 18 December 2017
Available online 04 January 2018
1877-7821/

diagnosis to the survivorship and surveillance phase, patients and their families will make multiple trips to medical professionals. Previous research has shown that rural patients experience greater disruptions in school, work and other obligations than their urban counterparts for cancer care [9,11–17].

One of the rural states facing these issues in pediatric cancer care is Nebraska, which is the 15th largest state covering 77,355 square miles [18,19]. Data from the National Cancer Institute 's SEER Program and the National Program of Cancer Registries reveal that the average incidence of pediatric cancer in Nebraska exceeds the national average for 2009 to 2013 (19.3 versus 17.4 per 100,000) [20–22]. Over one third of Nebraska residents live in a rural area, but pediatric cancer care for the entire population is provided only in the urban area of Omaha in the eastern part of the state. Consequently, many patients and their families need to travel a long distance to seek care. Furthermore, concerns about the potential effects of environmental factors (e.g., pesticide, agricultural run-offs) on pediatric cancer rates have been debated [23]. Nebraska is one of the leading agriculture states, ranking 4th in total agriculture receipts [24]. In 2016, 48,400 farms were in operation in Nebraska with over 45,000,000 acres utilized by operating farms [24].

Considering the challenges in pediatric cancer care due to the rural nature of the state, and recent data from SEER indicating an increased incidence of pediatric cancer in Nebraska in recent reporting periods, we sought to evaluate the incidence of pediatric cancer in Nebraska by comparing the state registry data to a nationally representative sample from the Surveillance, Epidemiology, and End Results (SEER). We hypothesized that pediatric cancer incidence within the State may vary by location given the existence of some urban areas amidst the large distinctive rural areas of the State. Given that pediatric cancer is a rare event, we evaluated 24 years of registry data to ensure the validity of our statistics. Geographic Information System (GIS) mapping was employed to display the spatial distribution of children with cancer in the state. Finally, we used our data to develop a strategy to improve the access to care for rural populations in Nebraska and identified a potential secondary site for a pediatric cancer care center.

2. Methods

2.1. Study design and data sources

This was a retrospective cohort study using the Nebraska Cancer Registry (NCR) and SEER 9 Registries as data sources. The NCR received gold certification from the North American Cancer Registry for 95% case ascertainment, ensuring the reliability of the analysis results [25]. SEER 9 registries research data (2015 November submission [20]) cover areas including San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta [26].

2.2. Case definition

Cases were restricted to children and adolescent patients (0–19 years) diagnosed with a primary malignant neoplasm between year 1990 and 2013. Diagnoses were grouped into 12 main groups by histology and primary site according to SEER Site/Histology Recode based on the International Classification of Childhood Cancer Third Edition (ICCC-3) and the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) [27]. We included in situ and malignant cases for urinary bladder cancer (ICD-O-67.9) to be consistent with other SEER reports [28]. To analyze the brain and CNS cancers, we also evaluated benign and uncertain cases for 2004- 2013.

2.3. Measures and data analysis

The following variables were examined in the analyses: age group, gender, and race/ethnicity. Due to the small size of certain races/ethnicities, race/ethnicity was re-coded as non-Hispanic white, non-Hispanic black, and other. Age was grouped into four categories: 0–4, 5–9, 10–14, and 15–19 years. Fisher exact test was used for comparing proportions between groups (NE versus SEER). All incidence rates (IRs) were calculated per million people and age-adjusted to the 2000 US standard population. IRs were displayed with 95% confidence intervals (CI) and compared with relative risk (RR) between Nebraska (primary group) and SEER (comparison group). All Nebraska IRs were calculated with SAS 9.4 [29] by using bridge-race population estimates prepared by the U.S. census Bureau and the National Center for Health Statistics [30]. SEER IRs were calculated with SEER*Stat, version, 8.3.2[31]. Due to restriction of race and ethnicity in SEER 9, age-adjusted IRs (AARs) by race and ethnicity groups were retrieved by using SEER 13 [26], which restricted the year of interest to 1992–2013. For the trend analysis, annual percentage change (APC) was calculated by fitting a regression line to data where the dependent variable was the natural logarithm of the data and calendar year was the independent variable. SEER*Stat was used to generate APCs and corresponding CIs for Nebraska data and SEER data. Trends of Nebraska pediatric cancer incidence were shown against national pediatric cancer incidence trends represented by SEER.

Location–Allocation analysis (LAA) of ArcGIS version 10.5 [32] was employed to determine a secondary site that would decrease the burden of travel from rural communities. To obtain possible facility locations, we started with existing pediatric cancer centers and added potential new facility locations based on existing adult cancer centers in the study area. With network/impedance, facility locations, and demands (locations of existing or potential cancer patients), the LAA can select the best candidate location to reduce travel time for patients and their family in the study area. Such selection was based on the calculations of LAA using alternative demands: first with the pediatric cancer patient's addresses and second with the existing child population at county centroids. This study was approved by the University of Nebraska Medical Center Institutional Review Board (543-15 EP).

3. Results

3.1. Demographics and tumor patterns of pediatric cancer patients

Of the 2094 pediatric cancer patients identified in Nebraska during 1990–2013, similar to the pattern in the US (SEER data), more pediatric cancers were observed in the youngest (0–4 years) and oldest (15–19 years) age groups (Table 1). A higher proportion of leukemias were observed at the oldest age (15–19) group in Nebraska (21%) compared to the US (15.4%) ($p = 0.001$). This age trend was also true for all pediatric cancers, lymphoma and CNS tumors. The race distribution of pediatric cancers was different between Nebraska and US SEER, underlining a predominance of non-Hispanic white patients in Nebraska.

3.2. Incidence rates of pediatric cancers in Nebraska versus US SEER

In general, the incidence of all and individual pediatric cancers was slightly higher in Nebraska compared to the US SEER population, however, the relative risk was within the 95% confidence intervals (Table 2). AAR of all pediatric cancers was 173.3 per million in Nebraska compared to 167.1 per million in the US SEER population. The AAR for lymphoma was significantly higher in Nebraska (28.1 per million vs. 24.6 per million; $p = 0.009$). Interestingly, for the oldest (15–19) age group, the age-specific rates for all and three most common pediatric cancers were higher in Nebraska compared to US SEER (Table 2). The IR for leukemias in 15–19 year-old patients was 33.7 per million in Nebraska compared to 25.9 per million in US SEER (RR = 1.3, 95% CI = 1.1–1.6). Similarly, the IRs for lymphomas and CNS tumors were higher in Nebraska compared to US SEER (RR = 1.2, 95% CI = 1.0–1.4 for lymphoma and RR = 1.3, 95% CI = 1.0–1.6).

The AARs of overall pediatric cancers differed by sex, with males showing higher incidence than females in both populations (Table 2).