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Epidemiology of oral, salivary gland and pharyngeal cancer in children and adolescents between 1970 and 2011

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ABSTRACT

Objectives: The age of oral and pharyngeal cancer patients has reportedly decreased over the last decade, but most of the peer-reviewed literature regarding oral and pharyngeal cancer in individuals 0–19 years of age (Y) is limited to specific tumor sites and/or types, or a small number of cases. Our aim is to characterize oral, salivary gland and pharyngeal cancer (OSPC) in 0–19 Y in order to improve knowledge of the disease in young individuals.
Methods: Data on OSPC between 1970 and 2011 was taken from the Israel National Cancer Registry, and included patient age, gender, tumor site and tumor type. Data analysis was performed by using IBM SPSS, Winpepi software and Joinpoint Regression Program. alpha < 0.05 was deemed statistically significant.
Results: A total of 13,863 OSPC cases were diagnosed with 2.6% (N = 357) of 0–19 Y. The male to female ratio was 1.5:1. The rates of diagnosis decreased between 1991 and 2011 and were not significantly different between the genders. The nasopharynx was the leading tumor site (42.3%) followed by the salivary glands (20.5%), and both were more common in 14–19 Y. The tonsils and other pharyngeal sites were common among 0–13 Y. The main tumor types were lymphomas (20.7%) and carcinomas (19.9%).
Conclusions: The general characteristics of OSPC remained unchanged over the last four decades. This may imply that environmental factors have not had any effect. Males are affected more than females and might have a genetic predisposition for nasopharyngeal malignancy. Health care providers should be aware of the common sites and tumor types among children and adolescents.

Introduction

Oral and pharyngeal cancer is one of the most diagnosed cancers worldwide [1], and is usually diagnosed in those 40–70 years of age (Y) [2]. In the United States (US), the rates of diagnosis of oral and pharyngeal cancer in children and adolescents (0–19 Y) between 2007 and 2011, ranged from negligible $0.0_{/100\ 000}$ in 0–4 Y to $0.5_{/100\ 000}$ in 15–19 Y [3]. Similarly, between 1970 and 2006 in Israel, the proportion of all oral, salivary gland and pharyngeal cancer (OSPC) cases was the lowest in children and adolescents (2.7%, N = 317) [4]. In the US, Squamous Cell Carcinoma (SCC) constitutes about 90% of oral and oropharyngeal cases, mostly related to tobacco and alcohol consumption [5]. These two factors are much more weakly associated with head and neck cancer in the young [6]. During the last decade, and despite that patients younger than 20 years have not been reviewed, the age at diagnosis of oropharyngeal cancer has been reported to decrease [7,8]. This has been related to the detection of human papillomavirus (HPV) in younger individuals [7]. Therefore the aim of the current research is to examine the characteristics and trends of OSPC in a young population. Additionally, to the best of our knowledge, most peer-reviewed literature regarding 0–19 Y describes specific tumor sites and/or types, and generally presents small numbers of cases. Therefore, studying the abundance of data available to us this study may contribute to the current knowledge about OSPC epidemiology in 0–19 Y.

Abbreviations: %, percentage; ANOVA, Analysis of Variance; APC, annual percent change; BL, Burkitt's Lymphoma; CI, confidence interval; ERMS, Embryonal Rhabdomyosarcoma; HPV, human papillomavirus; ICD-10, International Classification of Diseases and Related Health Problems 10th Revision; INCR, Israeli National Cancer Registry; LEC, Lymphoepithelial Carcinoma; MEC, Mucoepidermoid Carcinoma; N, number of cases; OSPC, oral, salivary gland and pharyngeal cancer; P, probability value (p-value); PA, Pleomorphic Adenoma; RR, Rate Ratio; SCC, Squamous Cell Carcinoma; SD, standard deviation; SGO, Salivary Gland Origin; UDC, Undifferentiated Carcinoma; UMT, Unspecified Malignant Tumors; US, United States; WHO, World Health Organization; Y, years of age; ΔP, difference between proportions; η^2, Partial Eta squared; χ^2, Pearson's chi-square test.

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Methods

Individuals diagnosed with OSPC were identified in the Israeli National Cancer Registry (INCR) data, between the beginning of January 1970 and the end of December 2011. The INCR was established in 1960, and records all tumor diagnoses in the citizens of Israel. Documentation in the registry is based on primary tumor diagnosis. The research was approved by the Institutional Review Board of the Hadassah Hospital in Jerusalem, Israel (protocol code: 0377-13-HMO) and by the INCR. The data were directly conveyed from the INCR to the authors, and included demographic variables (age, gender) and clinical variables (tumor sites and types).

Data on tumor stage and laterality were completed in less half of the cases.

The median age was used to form two age groups. For statistical analysis the period was subdivided: 1970–1990 and 1991–2011.

Tumor sites were categorized according to their distribution and the International Classification of Diseases and Related Health Problems 10th Revision (ICD-10), as determined by the World Health Organization (WHO) [9]. The five categories of tumor sites are: Lips (ICD-10 codes: C00.0-C00.9), Tongue and Mouth cavity (C02.0-C02.9, C03.0-C06.9), Salivary glands (C07.9-C08.9), Tonsils and other pharynx (C01.9, C09.0-C10.9, C13.9-C14.8), Nasopharynx (C11.1-C11.9).

Tumor types were categorized according to characteristics and frequencies and based on the International Classification of Diseases for Oncology (ICD-O-3), determined by the WHO [10]. The eight categories of tumor types are: Lymphoma (ICD-O-3 codes: 9590/3-9727/3), Carcinoma subtypes (8010/3, 8020/3, 8021/3, 8082/3, 8090/3, 8201/3), Salivary Gland Origin (SGO) (8140/3, 8200/3, 8430/3, 8525/3, 8550/3, 8940/3), SCC (8070/3-8073/3), Sarcoma (8801/3, 8810/3, 8900/3, 8910/3, 8920/3), Unspecified Malignant Tumors (UMT) (8000/3, 8001/3), Adenoma (8140/0, 8323/0, 8550/1, 8940/0) and Other tumor types (8000/1, 8081/2, 8806/3, 8821/1, 8900/0, 8990/1, 9251/1, 9370/3, 9500/3, 9530/0, 9540/0, 9751/3, 9752/1, 9863/3, 9930/3). The final category includes tumor types without histological characteristics found in other categories.

In order to calculate diagnosis rates, data on the mid-year population of 0–19 Y for the years 1970–2011 were directly conveyed from the INCR to the authors. These data are based on population data from the Israeli Central Bureau of Statistics. Diagnosis rate is the number of diagnoses in a certain year divided by the mid-year population of the same year. The total cancer diagnoses among Israeli 0–19 Y were only available for the years 2000–2011 [11], and were used to calculate diagnosis proportion, which is the number of OSPC diagnoses divided by total cancer diagnoses.

Statistical analysis

Significance level determined at $\alpha < 0.05$. Statistical analysis was performed by using the software listed below:

(1) IBM SPSS (version 21.0) [12]: (A) Student's *t*-Test for comparing the means of two categories. The mean and its standard deviation (SD) are presented as: mean ± SD. (B) Comparing means of three categories and above: (B1) One-Way Analysis of Variance (ANOVA). (B2) Partial Eta squared (η^2) as the effect size measurement. (C) Association between categorical variables: (C1) Pearson's Chi-square (χ^2) Test. (C2) Cramer's V as the effect size measurement.

(2) WinPepi (version 11.50): (A) Cohen's d as the effect size measurement between means of two categories. (B) Sidak-adjusted correction of Pearson's χ^2 Test for comparing two categories of a certain variable, while considering the rest of its categories. (C) Comparison of diagnosis rates by Rate Ratio (RR) and its 95% confidence interval (CI). 95% CI is presented as: [lower boundary, upper boundary]. (D) Comparison of diagnosis proportions by difference (ΔP) and its 95% CI. In case when at least one diagnosis rate equals zero, the diagnosis rates were compared as ΔP.

(3) Joinpoint Regression Program (version 4.3.1.0): Examining possible increase or decrease trends of diagnosis rates by calculation of the annual percent change (APC) and its 95% CI. The *t* distribution was used by the software to determine the significance of the APC value.

Results

Out of all OSPC cases in Israel during 1970–2011 (N = 13,863), a total of 357 cases were diagnosed in 0–19 Y (2.6%), with an average of $8.5 \pm 3.8_{\text{Diagnoses/year}}$.

Age at diagnosis ranged from 0 Y (N = 7) to 19 Y (N = 32), and the mean age was 12.5 Y ± 5.3. Based on the median age (14 Y), two age groups were created: 0–13 Y (45.1%, N = 161) and 14–19 Y (54.9%, N = 196) (Table 1).

Males had more OSPC than females (60.2%, N = 215; 39.8%, N = 142, respectively) (Table 1), and no significant differences were found by age between the genders (Cohen's d = 0.02). Throughout the period, the diagnosis rates were not significantly different between males and females (Supplementary Table 1). Likewise, from 2000 to 2011, the proportions were similar between the genders (Supplementary Table 2).

The nasopharynx was the leading tumor site category in general (42.3%, N = 151) and in both age groups (Table 1). The salivary glands were the second most diagnosed (20.5%, N = 73) (Table 1). Most of the salivary gland tumors were in the parotid glands (52.1%, N = 38). The nasopharynx and the salivary glands were more frequent in 14–19 Y, while tumors in the tonsils and other pharynx were diagnosed more often in 0–13 Y (Table 1) (13.3Y ± 4.9, 14.1Y ± 4.2, and 9.2Y ± 5.3, respectively; One Way ANOVA, $P < 0.001$; $\eta^2 = 0.10$). Mean age in diagnosis of the tonsils, separately, was 9.4Y ± 4.3.

The most frequent tumor type categories were lymphoma (20.7%, N = 74) and carcinoma subtypes (19.9%, N = 71), followed by SGO (16.2%, N = 58) and SCC (14.0%, N = 50) (Fig. 1).

Out of all diagnoses, the leading specific tumor types were: Burkitt's Lymphoma (BL) (10.4%, N = 37), Mucoepidermoid Carcinoma (MEC) (8.1%, N = 29), SCC (8.1%, N = 29), and Embryonal Rhabdomyosarcoma (ERMS) (7.3%, N = 26).

Tumor sites and tumor types are significantly associated (Pearson's χ^2 Test, $P < 0.001$; Cramer's V = 0.49). In the nasopharynx, carcinoma subtypes were the leading category (41.7%, N = 63). Of these, Lymphoepithelial Carcinoma (LEC) (15.2%, N = 23) and Undifferentiated Carcinoma (UDC) (13.9%, N = 21) were the leading tumors. LEC was more diagnosed between 1970 and 1990 (N = 19) than between 1991 and 2011 (N = 6). In contrast, UDC was more diagnosed between 1991 and 2011 (N = 19) than from 1970 to 1990 (N = 3). This difference was significant regarding the nasopharynx (Sidak-adjusted correction, $P < 0.001$; Cramer's V = 0.44).

Lymphoma was more prevalent in the nasopharynx (20.5%, N = 31) and the tonsils (including other pharynx) (66.7%, N = 32). Of the lymphomas, BL constituted 43.4% (N = 13) in the tonsils and 10.6% (N = 16) in the nasopharynx. Sarcoma was more prevalent in the mouth cavity (25.4%, N = 17) and the nasopharynx (10.6%, N = 16). Of these, ERMS constituted 18.5% (N = 10) in the mouth cavity and 7.9% (N = 12) in the nasopharynx. Of SGO tumors, the MEC was the leading type (30%, N = 29), specifically in the parotid glands (36.8%, N = 14). Among 0–13 Y, lymphoma (31.3%, N = 50) and sarcoma (21.1%, N = 34) were the most frequent diag-