



Research Paper

# Are demographics associated with mucoepidermoid or acinic cell carcinoma parotid malignancies in children?

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## KEYWORDS

Pediatric parotid cancer;  
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**Abstract** *Objective:* To identify possible associations between patient demographics and parotid cancer histological type in pediatric patients.

*Methods:* Pediatric patients (ages: birth–18.0 years) in the Surveillance, Epidemiology, and End Results (SEER) database were included from 1973 to 2014 based on a diagnosis of mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland using the ICD O-3 codes of C07.9 and 8430 or 8550. Patients were classified into the following cohorts: <14 and 14–18 years of age based on the mean age at diagnosis.

*Results:* Three hundred and three pediatric patients were diagnosed with mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland within the SEER 18 registries. Female pediatric patients 14–18 years of age were 7.68 times more likely to have an acinic cell carcinoma (adjusted OR: 7.68 [95% CI: 2.01–29.44]). When stratified by histological type, 58.9% of female pediatric patients ≥14 years of age had an acinic cell carcinoma as compared to 37.3% of male pediatric patients ≥14 years of age, 36.5% of female pediatric patients <14 years of age, and 34.0% of male pediatric patients <14 years of age ( $P = 0.01$ ).

*Conclusions:* Based on this study, pediatric female patients between the ages of 14 and 18 years are the most likely cohort to have acinic cell carcinoma. The results of this study may assist providers during the work up of a pediatric patient with a suspected parotid malignancy.

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## Introduction

Pediatric parotid tumors are usually benign in nature, however a small percentage are malignant.<sup>1</sup> Mucoepidermoid carcinoma has been widely noted to be the most common parotid malignancy in pediatric patients.<sup>2–5</sup> Acinic cell carcinoma has been noted to be the second most common epithelial pediatric parotid malignancy.<sup>6–8</sup> Recently, differences in treatment have been noted between the two subtypes as Radomski et al<sup>9</sup> identified a higher percentage of pediatric patients with mucoepidermoid carcinoma of the parotid gland underwent surgery which involved facial nerve sacrifice as compared to pediatric patients with acinic cell carcinoma. Radomski et al<sup>9</sup> also noted a higher percentage of pediatric patients with mucoepidermoid carcinoma of the parotid gland received adjuvant radiation. Given treatment paradigms may exist for pediatric parotid gland malignancies based on histological type, identification of demographical factors that favor a diagnosis of a specific histological type may allow healthcare providers to discuss expectations regarding both the patient's cancer course and treatment.

While previous studies have assessed patient demographics and tumor characteristics for pediatric patients with parotid malignancies, identification of predictive factors that favor one histological type remain unknown. Therefore, our objectives are to identify pediatric patients with mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland registered within the Surveillance, Epidemiology, and End Results (SEER) database and to analyze patient demographic and tumor characteristics and their relation to histological type. By identifying a possible relationship between patient demographics, tumor characteristics, and histological type, we hope to help identify pediatric patients who may have a predilection towards a certain histological type of parotid cancer.

## Materials and methods

Data was obtained using the National Cancer Institute's SEER database. Patients from the SEER database were included from 1973 to 2014. The SEER 18 Registry Research Data (released April 2017, based on the November 2016 submission) was utilized. This study was exempted from review by the Office of Research Integrity of the Medical University of South Carolina. Given Radomski et al.'s recent study which identified the highest percentage of pediatric parotid malignancies other than mucoepidermoid carcinoma or acinic cell carcinoma to be 4.1%, this study included only pediatric patients diagnosed with a mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland.<sup>9</sup> Patients were included based on a diagnosis of mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland using the ICD-O-

3 codes of C07.9: parotid gland primary site and 8430: mucoepidermoid carcinoma or 8550: acinar cell carcinoma. Patients were included from ages birth–18 years based on the documented age at diagnosis. Cases were also grouped according to the age at diagnosis into the following cohorts: <14 years of age and 14–18 years of age based on the mean age at diagnosis of the total cohort.

All data analyses were performed with SPSS 24.0 (IBM Corporation, Armonk, NY), SigmaPlot 12.5 (Systat Software, San Jose, CA), and MedCalc software 16.8 (MedCalc Software bvba, Ostend, Belgium). All continuous variables were tested for normal distribution as determined by the Kolmogorov–Smirnov test. Categorical variables were summarized by frequency, percentage, and/or range. Comparisons of categorical variables were performed using a Chi-Square test to identify variables which contained statistically significant differences. Comparisons of continuous variables were performed using a Mann–Whitney test. To assess for a relationship between patient demographics or tumor characteristics and histological type, Pearson correlation tests were performed. Univariable/multivariable logistical regression analyses were performed to identify variables which had increased odds of having acinic cell carcinoma as compared to mucoepidermoid carcinoma and to control for potential confounding variables. A *P* value of <0.05 was considered to indicate a statistically significant difference for all statistical tests.

## Results

### Patient demographics

From 1973 to 2014, 303 pediatric patients were diagnosed with a mucoepidermoid carcinoma or an acinic cell carcinoma of the parotid gland within the SEER 18 registries. Most pediatric patients were diagnosed in adolescence with a total cohort mean age of 13.8 (range 3.0–18.0). When stratified by histological type, 78 (46.2%) patients with mucoepidermoid carcinoma were <14 years of age at diagnosis as compared to 43 (32.1%) acinic cell carcinoma patients (*P* = 0.01). Ninety-one (53.8%) patients with mucoepidermoid carcinoma were female as compared to 90 (67.2%) acinic cell carcinoma patients (*P* = 0.02) (Table 1). When combining age and sex and stratifying by histological type, 63 (58.9%) female patients 14–18 years of age had an acinic cell carcinoma as compared to 28 (37.3%) male patients 14–18 years of age, 27 (36.5%) female patients < 14 years of age, and 16 (34.0%) male patients < 14 years of age (*P* = 0.01) (Table 2).

### Tumor characteristics

Pediatric patients with acinic cell carcinoma had lower overall stage disease and less nodal involvement. Twenty-

**Table 1** Patient demographics.

Characteristic	Total	Mucoepidermoid Carcinoma	Acinic Cell Carcinoma	P-value
Cases (%)	303 (100)	169 (55.8)	134 (44.2)	
Mean Age (years, Range)	13.8 (3.00–18.00)	13.3 (3.0–18.0)	14.4 (5.0–18.0)	0.03
Age Category No. (%)				0.01
<14 years of Age	121 (39.9)	78 (46.2)	43 (32.1)	
14–18 years of Age	182 (60.1)	91 (53.8)	91 (67.9)	
Sex No. (%)				0.01
Male	122 (40.3)	78 (46.2)	44 (32.8)	
Female	181 (59.7)	91 (53.8)	90 (67.2)	
Race No. (%)				0.59
Unknown	5 (1.7)	3 (1.8)	2 (1.5)	
Asian	21 (6.9)	10 (5.9)	11 (8.2)	
Black	47 (15.5)	30 (17.8)	17 (12.7)	
White	230 (75.9)	126 (74.6)	104 (77.6)	
Overall Cancer Stage No. (%)				<0.001
I	63 (20.8)	24 (14.2)	39 (29.1)	
II	45 (14.9)	27 (16.0)	18 (13.4)	
III	19 (6.3)	16 (9.5)	3 (2.2)	
IV	14 (4.6)	13 (7.7)	1 (0.7)	
Unknown	162 (53.5)	89 (52.7)	73 (54.5)	
Cancer Grade No. (%)				<0.001
Well Differentiated, Grade 1	76 (25.1)	49 (29.0)	27 (20.1)	
Moderately Differentiated, Grade 2	101 (33.3)	81 (47.9)	20 (14.9)	
Poorly Differentiated, Grade 3	6 (2.0)	6 (3.6)	0	
Undifferentiated/Anaplastic, Grade 4	13 (4.3)	12 (7.1)	1 (0.7)	
Unknown	107 (35.3)	21 (12.4)	86 (64.2)	
Nodal Involvement				<0.001
No	199 (87.3)	106 (80.9)	93 (95.9)	
Yes	29 (12.7)	25 (19.1)	4 (4.1)	

Asian: Asian and Pacific Islanders, mm: millimeter.

**Table 2** Age and sex stratified by histology type.

Characteristic	Total	Mucoepidermoid Carcinoma	Acinic Cell Carcinoma	p-value
Cohort by Sex and Age No. (%) <sup>a</sup>				0.01
Males <14 years of Age	47 (100.0)	31 (66.0)	16 (34.0)	
Females <14 years of Age	74 (100.0)	47 (63.5)	27 (36.5)	
Males 14–18 years of Age	75 (100.0)	47 (62.7)	28 (37.3)	
Females 14–18 years of Age	107 (100.0)	44 (41.1)	63 (58.9)	

<sup>a</sup> Row percentages expressed.

four (14.2%) patients with mucoepidermoid carcinoma had overall stage I disease as compared to 39 (29.1%) patients with acinic cell carcinoma ( $P < 0.001$ ). Twenty-nine (17.2%) patients with mucoepidermoid carcinoma had overall stage III or IV disease as compared to 4 (2.9%) patients with acinic cell carcinoma ( $P < 0.001$ ) (Table 1). Eighteen (10.7%) patients with mucoepidermoid carcinoma had grade 3 or 4 tumors. Eighty-six (64.2%) patients with acinic cell carcinoma had an unknown cancer grade. Twenty-five (19.1%) patients with mucoepidermoid carcinoma had nodal involvement as compared to 4 (4.1%) patients with acinic cell carcinoma ( $P < 0.001$ ).

### Factors associated with histological type

Patients of older age or female sex were more likely to be diagnosed with an acinic cell carcinoma. Univariable hazard ratios based on age and sex were calculated in Table 3. Compared to female patients less than 14 years of age, female patients 14–18 years of age had an odds ratio (OR) of 2.49 (95% CI: 1.35–4.59) for having an acinic cell carcinoma. Compared to male patients 14–18 years of age, female patients 14–18 years of age had an odds ratio (OR) of 2.40 (95% CI: 1.31–4.41) for having an acinic cell carcinoma. Table 4 describes patient demographics and tumor

**Table 3** Univariable logistic regression analysis identifying race and age associations with pediatric acinic cell carcinoma of the parotid gland.

Variable	Univariable Analysis: Odds Ratio (95% CI)
Males <14 vs. 14–18 years of age	
Male patients <14 years of age	Reference
Male patients 14–18 years of age	1.15 (0.54–2.48)
Females <14 vs. 14–18 years of age	
Female patients <14 years of age	Reference
Female patients 14–18 years of age	2.49 (1.35–4.59)
Males 14–18 vs. Females 14–18 years of age	
Male patients 14–18 years of age	Reference
Female patients 14–18 years of age	2.40 (1.31–4.41)
Males <14 vs. Females <14 years of age	
Male patients <14 years of age	Reference
Female patients <14 years of age	1.11 (0.52–2.40)

characteristics and their odds of having an acinic cell carcinoma as compared to a mucoepidermoid carcinoma of the parotid gland. Upon multivariate analysis, female pediatric patients 14–18 years of age had an adjusted odds ratio (aOR) of 7.68 (95% CI: 2.01–29.44) for having an acinic cell carcinoma. The Pearson correlations between age at diagnosis and histological type and sex and histological type were  $r = 0.135$ ,  $P = 0.02$  and  $r = 0.162$ ,  $P = 0.01$  respectively.

### Discussion

When assessing a pediatric patient with a parotid mass, several factors are often taken into consideration regarding the clinical course and management of each patient. This study noted multiple interesting findings which may assist healthcare providers in identifying pediatric patients with a mucoepidermoid carcinoma or acinic cell carcinoma of the parotid gland. In this study, most pediatric patients were diagnosed in adolescence (mean age 13.8 years). Xu et al similarly noted a median age of 16 years at the time of diagnosis for pediatric patients with salivary gland neoplasms.<sup>10</sup> Based on our cohort stratification, 121 (39.9%) patients in this study were diagnosed below the age of 14 years. Interestingly, pediatric patients with acinic cell carcinoma of the parotid gland presented at an older age as

**Table 4** Univariable and multivariable logistic regression analysis identifying characteristics associated with pediatric acinic cell carcinoma of the parotid gland.

Variable	Univariable Analysis: Odds Ratio (95% CI)	Multivariable Analysis: Adjusted Odds Ratio (95% CI)
Age and Sex Category No. (%)		
Male patients <14 years of age	Reference	Reference
Female patients <14 years of age	1.11 (0.52–2.40)	1.97 (0.49–7.84)
Male patients 14–18 years of age	1.15 (0.54–2.48)	4.30 (1.13–16.41)
Female patients 14–18 years of age	2.78 (1.36–5.68)	7.68 (2.07–28.71)
Race No. (%)		
White	Reference	— <sup>a</sup>
Black	0.69 (0.36–1.31)	— <sup>a</sup>
Asian	1.33 (0.55–3.26)	— <sup>a</sup>
Unknown	0.80 (0.13–4.92)	— <sup>a</sup>
Overall Cancer Stage No. (%)		
I	Reference	Reference
II	0.41 (0.19–0.90)	0.53 (0.19–1.51)
III	0.12 (0.03–0.44)	0.12 (0.02–0.93)
IV	0.05 (0.01–0.39)	0.09 (0.01–1.88)
Unknown	0.51 (0.28–0.92)	0.68 (0.27–1.72)
Cancer Grade No. (%)		
Well Differentiated, Grade 1	Reference	Reference
Moderately Differentiated, Grade 2	0.45 (0.23–0.88)	0.44 (0.18–1.10)
Poorly Differentiated, Grade 3	0.0 (0-)	0.0 (0-)
Undifferentiated/Anaplastic, Grade 4	0.15 (0.02–1.23)	0.26 (0.03–2.41)
Unknown	7.43 (3.81–14.52)	22.16 (7.22–67.98)
Nodal Involvement		
No	Reference	Reference
Yes	0.18 (0.06–0.54)	0.58 (0.12–2.72)

<sup>a</sup> Dropped out of the final multivariate model.

compared to patients with mucoepidermoid carcinoma. A significant association via Pearson correlation was noted between age at diagnosis and histological type. Additionally, a majority of pediatric patients with parotid mucoepidermoid or acinic cell carcinoma were female in this study. Radomski et al.'s study of major salivary gland malignancies noted 59.6% of patients with parotid malignancies were female.<sup>9</sup> When stratified by histological type, a majority of acinic cell carcinoma pediatric patients were of female sex. However, no major sex predilection was noted for pediatric patients with mucoepidermoid carcinoma. A significant association via Pearson correlation was noted between age at diagnosis and histological type.

We hypothesized that older female pediatric patients are more likely to have an acinic cell carcinoma of the parotid gland. To examine this hypothesis, patients were combined according to age and sex and stratified by histological type. Our study noted a higher percentage of female patients  $\geq 14$  years of age had acinic cell carcinoma as compared to mucoepidermoid carcinoma. On univariate analysis, female patients 14–18 years of age had a higher odds of having acinic cell carcinoma compared to younger female patients and males. On multivariate analysis, female pediatric patient's ages 14–18 years of age were the most likely cohort to have acinic cell carcinoma. This data indicates, therefore, that for pediatric patients in which a parotid malignancy is suspected, the odds of having acinic cell carcinoma compared to mucoepidermoid carcinoma is highest in female pediatric patients 14–18 years of age who are diagnosed with a malignant parotid mass.

Pediatric patients with salivary gland malignancies are known to present at earlier stages as compared to adults.<sup>11–14</sup> Although most patients in this study presented with lower stage cancers, our study demonstrated that pediatric patients with mucoepidermoid carcinomas of the parotid gland had a higher percentage of overall stage III or IV cancers as compared to patients with acinic cell carcinomas. Allan et al. similarly noted a higher percentage of overall stage I cancers for patients with acinic cell carcinoma of the parotid gland as compared to patients with mucoepidermoid carcinoma.<sup>15</sup> Future studies may seek to continue to evaluate if pediatric patients with mucoepidermoid carcinoma of the parotid gland present with a higher stage cancer as compared to other histological types.

Although several results have been discussed, there are limitations that are to be noted within this study. First, although the SEER-registry is population-based, not all patients within the United States are registered in the database and thus biases may exist regarding the patient population. Second, while tumor grade was available for several patients in this study, a significant portion of patients with acinic cell carcinoma had tumor grades classified as unknown. Thus, additional information not registered in the SEER database regarding tumor grade may have led alterations in this study's results. Additionally, data regarding other histological types of pediatric parotid cancers were not analyzed. Other possible associations may exist between patient demographics or tumor characteristics and other histological types of parotid malignancies. Finally, the classification of primary malignant tumors of the salivary gland has changed over time based on the

World Health Organization's classification system.<sup>16</sup> Therefore, it is unclear as to whether these histological types would be classified differently had they been recently examined. Despite these limitations, the SEER database was utilized in this study as it allows for a large-population analysis of pediatric mucoepidermoid or acinic cell carcinoma parotid cases within the United States. The SEER database also provides the ability to examine patient demographics and tumor characteristics which were vital to our study's purpose.

## Conclusion

While mucoepidermoid carcinoma of the parotid gland is considered to be the most common malignancy in pediatric patients, certain patient demographic groups may be more likely to be diagnosed with an acinic cell carcinoma. Our study demonstrates that pediatric female's ages 14–18 years have the highest odds of all pediatric cohorts of having acinic cell carcinoma as compared to a mucoepidermoid carcinoma. Healthcare providers may utilize these associations in their work up of a pediatric patient with a parotid mass.

## Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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