

# **Epidemiology**

# **Bulletin**

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A Study of the Risk Factors of  
Major Salivary Gland Tumors

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## **A Study of the Risk Factors of Major Salivary Gland Tumors**

### **1. Introduction**

The epidemiology of major salivary gland tumors is one area yet to be developed in the study of cancers as major salivary gland tumors are different from other tumors of the digestive system. They are rarely seen, and of all malignant neoplasms, they occupy only less than 1%. Even among malignant neoplasms of the head and neck areas, salivary gland tumors occupy less than 10%.<sup>(3,8)</sup> They, though rare, involve various different tissue cell types.

Much work conducted in the country, whether descriptive studies or investigations of pathogens, is related to some common malignant neoplasms, but very few epidemiological data are available regarding salivary gland tumors.

Salivary gland tumors are never treated separately in the studies of tumors of the oral cavity (ICD 140-149). The salivary gland is an external secretory gland, the risk factors that induce salivary gland tumors may be different from those that induce other cancers of the oral cavity.

In the epidemiological study of cancers, one should not stop at what has already been done, and one should go a step further to study tumors which have never been studied. From the viewpoint of prevention, diseases either common or rare, should be prevented with equal care. The study intends to investigate the possible risk factors of the salivary gland tumors in Taiwan.

### **2. Materials and Methods**

#### **1) Data Collection (collecting data for cases and controls)**

Cases: 221 cases of salivary gland tumors, 132 males and 89 females, were collected from the Cancer Registration of the Department of Health for the year 1986-1988.

Controls: For each case, four neighbors were selected as controls. They are persons (1) living in the same Lin or same Li; (2) of the same sex; (3) of the age within the range of five years.

## 2) Interviewing

An interview was conducted by trained interviewers with a questionnaire. To avoid bias, interviewers were not told of the status, either case or control, of the interviewees. Questionnaire included items on the background of the interviewee, his disease history, occupational exposure, history of drinking, smoking, tea drinking, betel nut use, use of hairdyes, conditions of oral cavity, experience of x-ray exposure, and injuries on face. Only 100 cases had been successfully interviewed (63 males and 37 females) due to unavailability (not met on 3 visits), refusal and change of residence, etc. For controls, 285 had been interviewed (176 males and 109 females). Both cases and controls came from the 21 counties and cities of the Island. Of the 100 cases, 20 were already dead at the time of interview, their spouses or family members were interviewed instead. All controls were living at the time of interview.

## 3) Statistical Analysis

(1)  $X^2$ -test was used to test the difference. Where  $X^2$  value is equal to or less than 5, Fisher's exact test was applied to calculate the p-value. T-test was used to test the difference between averages.

(2) Mantel-Haenszel method was used to calculate the odds ratio and 95% confidence interval between variables of cases and controls. Mantel-Haenszel test was also used to calculate the M-H Summary Chi-Square in order to test the hypotheses.

## 3. Findings

### 1) Sex, age and Residence

In total, 385 persons (100 cases and 285 controls) had been interviewed at homes. Their sexes and ages are shown in Table 1. Of the 100 cases of salivary gland tumors, 63 were male and 37 female. No statistically significant difference in sex is seen between cases and controls ( $p=0.825$ ). The average age for cases is 53.32 years ( $\pm 14.10$  years), and that for control is 52.68 ( $\pm 14.31$ ). Again, no difference is seen ( $p=0.699$ ).

They all come from the same areas (Table 2) at similar proportion. Of the 100 cases, 31 (31%) are from Taipei City, 12 from Taipei County and 10 from Tainan County.

### 2) Education and Martial Status

No difference is found either in the education ( $p=0.618$ ) or the marital status

( $p=0.102$ ) of cases and controls.

### 3) Birthplace, Blood Type and Religion

Of the 100 cases, 72 are of Fukien origin. No difference is found in birthplace between cases and controls ( $p=0.383$ ) (Table 3).

In blood types, 36 cases are of the O-type and 24 of B-type. Again, no difference is found in blood types between cases and controls ( $p=0.11$ ) (Table 3).

In terms of religion, 49 of the 100 cases were Taoists and 33, Buddhists. When both cases and controls are grouped under Christians, Catholics, Buddhists, Taoists and none, some difference is found ( $p=0.037$ ). However, when Christians and Catholics are grouped together, no difference in religion between cases and control is seen ( $p=0.789$ ).

### 4) History of Disease

As shown in Table 4, diseases of the lymphatic gland (O.R.=8.23, 95% C.I.=2.88–26.57,  $p$  0.01) and stone of the slivary gland (O.R.=18.47, 95% C.I.=2.18–852.35,  $p$  0.01) show statistically significant differences between cases and controls. No differences, however, are found in diseases such as diseases of the thyroid gland, diseases of liver and gall, diabetes, heart diseases, hypertension, arthritis, erythroderma, diseases of selfimmunity, allergic dermatitis, frequent inflammation of tonsil, diseases of internal secretion, diseases of pancreas, mumps, nasosinusitis and diseases of the lachrymal gland.

### 5) Some X-ray, Hairdyes and Injuries of Face

Only the exposure of either head or neck to x-ray shows some significant difference between cases and controls (O.R.=8.25, 95% C.I.=4.70–14.48,  $p$  0.001). Others such as the use of hairdyes and injuries of face show no difference between cases and controls (Table 5).

### 6) Smoking, Alcohol Drinking, Tea Drinking, and Betelnut Chewing

No significant differences between cases and controls are found in terms of these habits.

### 7) Occupational Exposure

The exposure to organic solvents shows a statistically significant difference between the two groups (O.R.=0.13, 95% C.I.=0–0.86,  $p$  0.05), that is organic solvents seem to be protective. This is probably due to the small size of the samples. Other experiences such as exposures to sunlight, dyes and other chemicals do not show any differences between the two groups (Table 6).

#### 8) Conditions of Oral Cavity

No difference is found between cases and controls in terms of mouth-rinsing, periodical removal of dental stones, rinsing after meals, frequency of tooth-brushing, uneven arrangement of teeth and bad breath.

### 4. Discussion

While factors that may induce salivary gland tumors are not yet clear, the effects of some suspected factors on the mechanism of salivary gland tumors are not supported academically. Under the circumstances that the biological evidences are insufficient and that the time-order of correlation can not be determined, the findings of the present study cannot effectively establish the cause-effect relations of some suspected risk factors and the salivary gland tumors. Some of the findings and the limitation of study are discussed as follows.

#### 1) Limitations of study

##### (1) The memory bias of interviewee

This is a common problem of control group studies and has many impacts on the findings as well. When interviewees were asked, for instance, of the diseases of their parents, most cases as well as controls would reply that they were not certain. During the interview, some cases had died, their spouses or family members were interviewed instead. Their statements of the personal habits of the deceased were hard to confirm.

(2) The interview took at least 40 minutes to complete. It took place at the interviewee's home. Often, both the interviewer and interviewee became impatient and the interview was ended in a hurry. Though the interviewers work hard, the responses obtained under these circumstances could not be guaranteed of their accuracy.

##### 2) The Risk Factors

The study has found that persons who have had diseases of the lymphatic gland are more likely to develop salivary gland tumors. This fact has never been mentioned in any international literature. The significant difference in the diseases of lymphatic gland between the two groups obtained by the present study, perhaps, is due to the fact that malignant salivary gland neoplasms often transfer to the lymphatic gland to become problems of the lymphatic gland. In addition, the interviewers asked about diseases of any lymphatic gland of the body rather than focussing on the head and neck area in their interview.

The study also shows a statistically significant relation between salivary gland stones and salivary gland tumors. This fact, again, has not been mentioned in any international literature. While the symptoms of salivary gland stones are not

easily defined, we suspect that interviewees took salivary gland stones for salivary gland tumors while responding to the questionnaire.

Our findings show that exposure of the head and neck area to x-ray is an important risk factor. This fact has been mentioned in international literature. In fact, x-ray exposure is the only risk factor that has been discussed in detail. The risk was indicated even in the earlier follow-up studies of the survivors of the atomic bombs in Japan around the end of the 2nd World War.<sup>(1,2)</sup> This relation also appears in children under radiation therapy.<sup>(4,5,6)</sup> To avoid any biases resulting from subjective judgement by the interviewers, they were not told of the status, either cases or controls, of the persons interviewed. Therefore, while they were on the question of exposure of head and neck to x-ray, they could not probe the cases further as to whether their heads and necks had been exposed to x-ray at least a year before their salivary gland tumors were diagnosed. The findings thus could be over-estimated.

Spitz's<sup>(9)</sup> study shows that persons of higher social-economic status and educational level have higher risks, while other studies, however, do not show any relationship between these factors and salivary gland tumors. The present study finds no statistically significant difference in these factors between cases and controls.

Smoking has not been found to be a risk factor.<sup>(7,10)</sup> The incidence of salivary gland tumors and smoking rate do not show any ecological relation. Smoking is not found to be a risk factor in the present study, either.

Betel-nut chewing is not found to be a risk factor in the present study. Though betel-nut chewing has not been mentioned in international literature, the findings of the present study are quite reasonable. Betel-nut chewing is considered a risk factor for the cancer of the oral cavity, and it works mainly on the mucus of oral cavity to induce change of the mucus. The whole process of betel-nut chewing is not directly related to the salivary gland. Betel-nut chewing, therefore, is probably not a risk factor for the salivary gland tumors. On the other hand, salivary gland opens into the oral cavity, it should have some contact with betel-nut. Betel-nut chewing also is considered to stimulate the secretion of saliva.

## 5. Conclusions

The present study of the risk factors related to salivary gland tumors has shown statistically significant differences between cases and controls in whether individuals have suffered from diseases of the lymphatic gland and stones of the salivary gland, and whether individuals have been exposed to x-ray. Though there are inevitable limitations to the present study, the findings of the study can be of some value, and would hopefully encourage more studies on this subject.

**Prepared by:** T.L. Cher<sup>1</sup> R.H. Lin<sup>2</sup> and K.T.<sup>1</sup> Chen (1. FETP, National Institute of Preventive Medicine, Department of Health; 2. Institute of Public Health, National Taiwan University).

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**Table 1. Age and Sex Distribution of Cases and Controls**

	Cases	Controls
	No. (%)	No. (%)
Age:		
≤ 35	14 ( 14)	45 ( 16)
36-45	17 ( 17)	42 ( 15)
46-55	18 ( 18)	51 ( 18)
56-65	32 ( 32)	91 ( 32)
66-75	16 ( 16)	50 ( 17)
≥ 76	3 ( 3)	6 ( 2)
Total	100 (100)	285 (100)
Sex:		
Male	63 ( 63)	176 ( 61)
Female	37 ( 37)	109 ( 39)
Total	100 (100)	285 (100)

**Table 2. Geographic Distribution of Cases and Controls**

	Cases	Controls
	No. (%)	No. (%)
Keelung City	5 ( 5)	15 ( 5.2)
Taipei County	12 ( 12)	42 ( 14.7)
Ilan County	1 ( 1)	2 ( 0.7)
Hsinchu County	3 ( 3)	6 ( 2.1)
Taoyuan County	1 ( 1)	2 ( 0.7)
Miaoli County	2 ( 2)	4 ( 1.4)
Taichung County	7 ( 7)	28 ( 9.8)
Changhua County	6 ( 6)	20 ( 7 )
Tainan City	3 ( 3)	4 ( 1.4)
Tainan County	10 ( 10)	38 ( 13.3)
Kaohsiung County	1 ( 1)	2 ( 0.7)
Penghu County	1 ( 1)	2 ( 0.7)
Pingtung County	5 ( 5)	18 ( 6.3)
Taitung County	2 ( 2)	1 ( 0.3)
Hualien County	4 ( 4)	16 ( 5.6)
Taipei City	31 ( 31)	88 ( 23.8)
Hsinchu City	3 ( 3)	3 ( 1 )
Chiayi City	2 ( 2)	8 ( 2.8)
Kaohsiung City	1 ( 1)	1 ( 0.3)
Total	100 (100)	285 (100 )

**Table 3. Birthplace, Blood-Type and Religion Distribution of Cases and controls**

	No. of Cases	No. of Controls	P-value
Birthplace:			
Fukienese	72	170	
Hakka	8	37	NS
Aboriginal	2	5	
Mainlander	17	36	
Blood-Type:			
A	21	60	
B	24	47	NS
AB	8	15	
O	36	140	
Religion:			
Christian	2	15	
Catholic	6	3	*
Buddhist	33	81	
Taoist	49	151	
None	10	30	

\*  $p < 0.05$ 

NS: not significant

**Table 4. Disease History of Cases and Controls**

		Case	Control	Odd Ratio	95% CI	P-value
Diseases of internal secretion	yes	2	4	1.48	0.13–10.54	NS
	no	90	267			
Diseases of pancreas	yes	2	9	0.62	0.90–3.12	NS
	no	95	263			
Diseases of lymphatic gland	yes	15	6	8.23	2.88–26.57	**
	no					
Salivary gland stone	yes	6	1	18.47	2.18–852.35	**
	no					
Mumps	yes	10	27	1.06	0.46–2.42	NS
	no					
Nasosinusitis	yes	7	18	1.10	0.40–2.90	NS
	no	92	260			
Frequent inflammation of tonsil	yes	1	17	0.16	0.00–1.06	NS
	no	97	266			
Diseases of lachrymal gland	yes	4	11	1.03	0.27–3.6	NS
	no	94	266			

\*\* p &lt; 0.01

NS: not significant

**Table 5. X-ray Hairdyes and Injuries of Face of Cases and Controls**

		Case	Control	Odd Ratio	95% CI	P-value
Hairdyes	yes	29	74	1.15	0.66–1.95	NS
	no	71	208			
Exposure of head and neck to x-ray	yes	58	42	8.25	4.70–14.48	**
	no	37	221			
Injuries on face	yes	4	17	0.66	0.16–2.09	NS
	no	92	257			

\*\* p &lt; 0.01

NS: not significant



**Table 6. Occupational Exposures in Cases and Controls**

		Case	Control	Odd Ratio	95% CI	P-value
Exposure to sun	yes	20	66	0.88	0.47–1.60	NS
	no	69	201			
To organic	yes	1	21	0.13	0–0.86	*
	no	88	246			
To dyes	yes	3	2	4.57	0.51–55.26	NS
	no	86	262			
Other chemicals	yes	3	7	1.32	0.21–5.92	NS
	no	84	258			

\*  $p < 0.05$

NS: not significant