

Determining the Association of Benign and Malignant Salivary Gland Tumours with ABO-Rh Blood Groups

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ABSTRACT

Introduction:

Various studies have proposed that some ABO blood groups may be associated with increased risk of cancer. Hence, we decided to conduct this study to investigate the relationship between ABO-Rh blood group and risk of salivary gland tumor.

Materials and Methods:

In this study, 190 patients with salivary gland tumor and 400 healthy persons were investigated. Demographical information including ABO blood group of both groups were collected and analyzed using the SPSS 18 version. Binary logistic regression (univariate and multivariate model) were applied with 95% confidence interval.

Results:

The most common blood group in patients with salivary gland tumor was blood group O. There was no significant relationship between the ABO blood group and salivary gland tumor risk (All; $p > 0.05$). The blood group O and A were the most abundant blood groups in patients with the malignant and benign salivary gland tumor respectively (46.6%, 35.7%). The risk of malignancy of tumor in the patients with blood group O was marginal (1.84; 95%CI: 0.96-3.53, $p: 0.06$).

Conclusion:

This study shows no relationship between ABO-Rh blood groups and salivary gland tumor risk. However, to reach a definitive conclusion about the risk of malignancy in blood group O, stronger studies are needed in the future.

Keywords:

Salivary Gland Neoplasms; Blood-Group

Salivary gland tumors (SGT) constitute about 1-5% of all head and neck tumors. The annual incidence of SGT is different in different parts of the world, ranging from 0.5 to 2 per 100,000.¹ Tumors are mostly located in the major glands, especially in the parotid gland; 10% to 20% occur in the minor salivary glands.² Majority of these, almost 80%, are benign and only 20% are malignant. The prevalence of malignant tumours is 20-25% in the parotid glands, 40% in the submandibular glands, and about 90% in sublingual gland.^{1,3} The most common cancer is mucoepidermoid carcinoma in the parotid glands and adenoid cystic carcinoma in the submandibular and minor salivary glands.⁴

SGTs, in both the major and minor salivary glands, often present as enlarging masses without pain. The majority of these tumors can be treated with surgical excision alone, while adjuvant therapy in the form of chemoradiotherapy may be required for high-grade

tumors and advanced tumours with metastasis.

Most head and neck cancers are strongly etiologically related to lifestyle factors such as smoking, alcohol consumption and diet. But based on present knowledge, these agents do not play a role in SGTs. Factors such as employment at rubber manufacturing units, woodworking, hairdressing, history of Epstein-Barr virus infection, immunosuppression, cancer and radiation may be related with SGTs.^{5,6}

Cancer is multifactorial; besides lifestyle and environmental factors, genetics and heredity have important role in causing cancer.

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Various studies have proposed the relationship between the ABO blood groups and some cancers.⁷⁻¹¹ The first report, about association between gastric cancer and blood group A was published in 1953.¹² The antigens of blood groups are widely expressed on the membranes of red blood cell, epithelia, platelets, sensory neurons and vascular endothelia, and also body fluids.¹³ Underlying mechanisms of this association are unclear. There is growing evidence regarding role of ABO blood group in the development of neoplastic and other disorders.^{7,13-15}

Based on literature review, there is paucity of studies about association between SGTs and ABO blood groups. There were conflicting reports about the relationship between the ABO blood groups and these tumors.^{16,17} Therefore, we decided to conduct this study to evaluate the relationship between SGT and ABO blood group.

Material and Methods

A total of 190 patients with salivary gland tumor who were admitted between March 2007 and September 2017 and consented to participate, were enrolled in the study. All patients had definitive diagnosis of a salivary gland tumor based on International Classification of Diseases for oncology (ICD-O)-10th edition. Patients with any other malignant diseases were excluded. A control group was selected from outpatients visiting the hospital during the same period as the case group but having no evidence of salivary gland diseases or any cancer. The number of control subjects was 400 (two controls for each case). Detailed information of the cases such as gender, age, history of smoking, and ABO blood group were obtained from the medical records. In control group, in addition to similar information, the blood group was determined.

Statistical Analysis:

Independent t- test was applied to compare quantitative variables without skewed distribution. Chi square test was used to compare the proportions. The study population was categorized into two groups based on age with 60 years being the watershed line. The proportions of ABO blood groups were compared between case and control groups. We conducted unconditional logistic regression

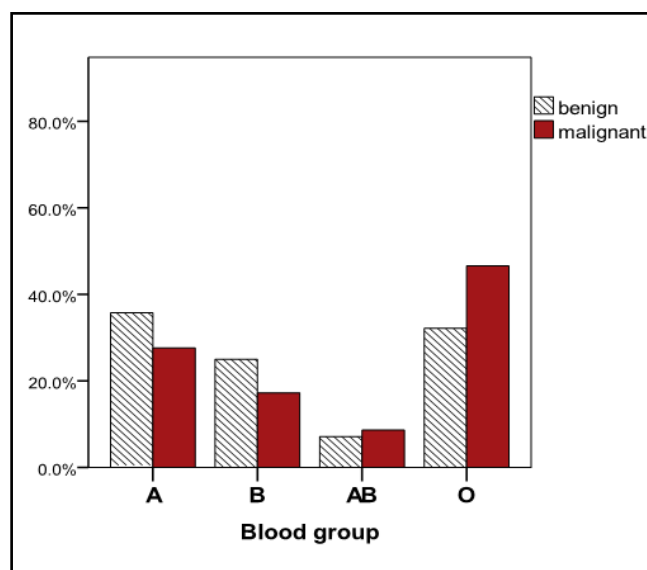


Fig. 1: ABO distribution in the patients with benign / malignant salivary gland tumor

to determine the association between ABO blood group and risk of SGT (with 95% CI). We calculated odds ratios in age groups after adjusting for gender. We analyzed separately the cases based on nature of tumor (benign or malignant) and assessed the relationship of those tumors with ABO blood groups. All statistical analyses were performed with SPSS version 18 for Windows.

Results

Overall study groups:

This study investigated 190 patients with SGTs and 400 controls. Majority of the cases were male (58.4%). The mean age was 45.6(\pm 17.3) years for case group and 47.0(\pm 7.7) years for control group. Of the cases, 34.3% were smokers and 5% had past history of alcohol consumption. Table I shows the characteristics of cases and controls, and demonstrates no statistically significant differences in studied variables between the two groups except age. The proportion of persons 60 years of age or older was higher in case group than control group (22.5 vs. 4.5%, Odds ratio: 6.15; 95% CI: 3.43-11.03, $p < 0.001$).

ABO blood group and risk of salivary gland tumours:

Of the case group, only for 170 patients, ABO blood group was recorded in medical profile. Sixty-three (37.1%) had blood group O, 59 (32.9%) had blood group A, 38 (22.4%) had blood group B and 13 (7.6%) had blood group AB. No statistically significant relation was found between SGT and ABO blood groups. (Table I) The proportion of ABO blood groups in the control group was similar to Iranian population.¹⁸

The distribution of ABO blood groups in the cases group had significant difference based on age ($p:0.04$). The most common blood group in the cases < 60 years was blood group A (34.9%), and in the cases ≥ 60 years, it was blood group O (46.2%).

Table II shows the results of logistic regression analyses in two age groups adjusted for sex. We found

no significant relationship between ABO blood groups and SGT. The proportion of Rh blood group also did not have significant difference between case and control groups ($p:0.25$).

Of all the SGTs, 124 were benign (117 in parotid glands, 4 in submandibular glands and 3 in palate) and 66 were malignant (52 in parotid glands and 14 in submandibular glands).

We assessed some variables in the patients with benign and malignant tumours. (Table III) The results showed that the risk of malignancy in the patients with age ≥ 60 years was 2.02-fold of the risk in younger patients. The most common blood group in benign tumours was A ($n=40$, 35.7%) and in malignant tumours was O ($n=27$, 46.6%). (Fig. 1). Patients with blood

Table I: Baseline Characteristics of SGT cases and control group

VARIABLES	CASES (N=190)	CONTROLS (N=400)	CRUDE OR (95%CI)	P-VALUE
Age	45.6 \pm 17.30	47.0 \pm 7.77	1.011 (0.10-1.03)	0.17
Gender				
Male	111(58.4)	244(61.0)	1.113 (0.78-1.58)	0.59
Female	79(41.6)	156(39.0)	1	
Age group				
<60	147(77.4)	382(95.5)	1	<0.001
≥ 60	43(22.6)	18(4.5)	6.15(3.43-11.03)	
Smoking				
Yes	65(34.2)	110(27.5)	0.73(0.50-1.05)	0.1
No	125(65.8)	290(72.5)	1	
ABO blood group				
A	59(32.9)	144(36.0)	1.14 (0.78-1.67)	0.48
B	38(22.4)	74(18.5)	0.78 (0.51-1.23)	0.29
AB	13(7.6)	33(8.2)	1.08 (0.56-2.12)	0.81
O	63(37.1)	149(37.3)	1.00 (0.78-1.67)	0.97

Table II: The Risk of Salivary Gland Tumor and ABO-Rh blood group

VARIABLES	CASES (N=190)		CONTROLS (N=400)		CRUDE OR (95%CI)	P-VALUE
	NO.	%	NO.	%		
ABO (Age<60)						
O vs others	44	34.1	142	37.2	1.14 (0.75-1.74)	0.54
A vs others	45	34.9	137	35.9	1.03 (0.69-1.59)	0.84
B vs others	33	25.6	71	18.6	0.67 (0.42-1.08)	0.09
AB vs others	7	5.4	32	8.4	1.57 (0.67-3.65)	0.29
A+B+AB vs other	85	65.9	240	60	0.88 (0.58-1.33)	0.54
RH+	119	92.2	340	89	0.66 (0.32-1.35)	0.25
RH-	10	7.8	42	11	1	
ABO (Age>=60)						
O vs others	18	46.2	7	38.9	0.80 (0.31-2.45)	0.59
A vs others	10	25.6	7	38.9	1.91 (0.56-6.54)	0.3
B vs others	5	12.8	3	16.7	1.36 (0.29-6.44)	0.7
AB vs others	6	15.4	1	5.6	0.31 (0.03-2.84)	0.3
A+B+AB vs other	21	53.8	11	61.1	1.41 (0.41-4.88)	0.59
RH+	38	97.4	16	88.9	0.20 (0.02-2.48)	0.21
RH-	1	2.6	2	11.1	1	

Odds ratio (OR) was adjusted based on sex variable. The significant level was considered less than 0.05.

group O had marginally increased risk of malignancy compared to non-O blood groups (Odds ratio: 1.84; 95% CI: 0.96-3.53, p: 0.06). Other blood groups did not definitely have a significant relationship, after adjusting for age and sex. (Table III)

Discussion

Recently, various studies have been performed for showing the association between blood groups and risk of cancer. A few studies have also been done on the relationship between salivary gland tumors and ABO blood group.

In this study, we observed the same relative frequency

of blood groups A and O in cases with age younger than 60 years old and the blood group O was found to be predominant in older age. However, there was no statistically significant relationship between ABO blood groups and SGT. Pinkston et al.¹⁹ and Garret et al.¹⁶ reported no relationship between SGT and ABO blood group; Pinkston has rather reported a lower percentage of blood group A in cases than control group.¹⁹ Osborne et al. showed this relationship and also reported a high incidence of SGT in blood group A.¹⁷ In contrast to our study, they found blood group A as the most common group in the patients followed by group O. A recent systematic review and meta-analysis suggested that blood group A was associated with increased cancer incidence; however these results had a limitation for

Table III: The comparison between benign and malignant tumor

VARIABLES	BENIGN	MALIGNANT	OR(95%CI)	P-VALUE
Sex (n,%)				
Male	72(64.9)	39(35.1)	1.04 (0.57-1.91)	0.89
Female	52(65.8)	27(34.2)	1	
Age group (n,%)				
Age<60	100(69.0)	45(31.0)	1	0.04
Age>=60	22(52.4)	20(47.6)	2.02 (1.00-4.07)	
Smoking (n,%)				
Yes	43(66.2)	22(33.8)	0.94 (0.50-1.77)	0.85
No	81(64.8)	44(35.2)	1	-
Anatomical Site (n,%)				
Parotid	117(69.2)	52(30.8)	1	-
Sub maxillary	4(22.2)	14(77.8)	4.50 (1.71-11.80)	<0.001
Accessory	3(100.0)	0(0.0)		
Side (n,%)				
Left	74(69.8)	32(30.2)	0.64 (0.35-1.16)	0.14
Right	48(59.3)	33(40.7)	1.58 (0.87-2.89)	0.13
Bilateral	2(66.7)	1(33.3)	0.99 (0.08-10.55)	0.94
Size (mean ± sd.) cm	3.2 ± 1.5	4.5 ± 3.0	1.29 (1.09-1.53)	<0.001
Duration (median, range)month	24(1,300)	12(1,240)	0.99 (0.98 -1.00)	0.34
ABO blood group (n, %)*				
A vs others	40(71.4)	16(28.6)	0.69 (0.34 - 1.37)	0.27
B vs other	28(73.7)	10(26.3)	0.67 (0.29 - 1.59)	0.35
AB vs others	8(61.5)	5(38.5)	1.07 (0.32 - 3.56)	0.91
O vs others	36(57.1)	27(42.9)	1.84(0.96 - 3.53)	0.06
RH+	103(64.8)	56(35.2)	2.29(0.47 - 11.15)	0.3
RH-	9(81.8)	2(18.2)	1	

*Odds ratio of blood group were adjusted for sex and age group. The significant level was considered less than 0.05.

SGT, because only one study was included in this analysis.¹⁰ In another recent study, Singh et al. had a near agreement with our results; they have reported a more or less even distribution of ABO blood group in patients with SGT and the most common blood group was blood group O.⁷

On the other hand, we found, by univariate and multivariate analyses, that blood group O might be a risk factor for malignancy in the patients with SGT. The blood group O had been reported as a poor prognostic factor for the patients with laryngeal cancer, whereas it was found a protective factor in the patients with nasopharyngeal carcinoma and other cancers.^{8,13,20} Osborne et al in their study found high frequency of blood group A in malignant SGT. We calculated odds ratio using data of that study for comparison, so odds ratio of malignancy for blood group A was 1.133 (95%CI: 0.80-1.60) and for blood group O was 0.923(95%CI: 0.64-1.31). These results were not significant, but it was almost borderline for blood group A in Osborne study. However the prognostic value of ABO blood group have been suggested in cardiovascular diseases and some cancers, but the evidence is not enough and it requires more studies to understand underlying pathophysiological mechanisms.¹³

ABO antigens were discovered in the early 1900s. These antigens are expressed on red blood cells, platelets, epithelial and endothelial cells. Aird et al in 1953, suggested the association between ABO blood group and risk of gastric cancer.¹² Moreover, various studies have corroborated this possible association. It was discussed that this observed association cannot be due to ABO blood antigens, but they may have an effect on genes located close to ABO blood group genes. The underlying mechanisms have been proposed to explain these findings, but the main molecular mechanisms are still unknown, and scientific research on this subject is growing. Since the distribution of ABO blood group can widely vary among different races and ethnicities in the world,^{21,22} more studies are needed in various regions of the world with different head and neck cancers.

The limitations of our study should be accepted. First, the number of the patients with accessory salivary gland tumours was few. Second, our study was conducted in a single center, and our participants enrolled mostly from

Tehran province. To further investigate the borderline risk of blood group O, it can be conducted in other settings with appropriate sample size including more accessory salivary gland tumours.

Conclusion

Our results showed no relationship between ABO-Rh blood group and salivary gland tumour. But considering wide genetic differences among people in different parts of the world and environmental factors, it is suggested to do further studies in other populations to confirm or disapprove our findings.

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