

ANALYSIS OF ARCHIVE MATERIAL OF PATIENTS WITH SALIVARY GLAND NEOPLASMS ACCORDING TO THE DEPARTMENT OF O.O. BOGOMOLETS NATIONAL MEDICAL UNIVERSITY FOR THE LAST FIVE YEARS

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ABSTRACT

INTRODUCTION: The frequency of salivary gland tumours remains high enough to date from 1% to 5% of all human tumours. Among benign tumours, pleomorphic adenomas dominate from 61% to 90%, and among malignant tumours, adenocarcinomas – 20%.

OBJECTIVES: The purpose of our research was to evaluate an analysis of archive material of patients with neoplasms of the salivary glands that were treated at the department of O.O. Bogomolets National Medical University in the last five years.

MATERIAL AND METHODS: The material for the survey were archival histories of 232 patients with neoplasms of the salivary glands. The average age of patients was 50 ± 15.3 years. All patients underwent general clinical examinations. All patients were given a typical surgical intervention – excisional biopsy, partial, subtotal, or total parotidectomy. Postoperative material passed the pathohistological study.

RESULTS: Analysis of archival histories of patients with neoplasms of the salivary glands in the period 2014–2018 shows that most of the pathohistological diagnoses were: pleomorphic adenomas 133 (57.32%), adenocarcinomas 48 (20.68%), and adenolymphomas (Warthin tumour) 33 (14.22%). The analysis of data on the distribution of patients by type of malignant tumours of the salivary glands showed that the largest number of patients was with mucoepidermoid cancer and acinic cell adenocarcinoma in 16 (33.33%) and 12 (25%) patients, respectively.

CONCLUSIONS: In this article we discussed most of the statistics associated with salivary gland neoplasms, such as frequency of salivary gland tumours (benign and malignant), distribution of patients by gender and age, localisation of pathological process, non-coincidence of clinical and pathological diagnoses, histological types of pleomorphic adenomas, and their distribution depending on age and gender.

KEY WORDS: salivary gland tumours, pleomorphic adenoma, adenocarcinoma, histological types of pleomorphic adenomas.

J Stoma 2019; 72, 2: 70–76

DOI: <https://>

**JOURNAL OF
STOMATOLOGY**
CZASOPISMO STOMATOLOGICZNE

OFFICIAL JOURNAL OF THE POLISH DENTAL ASSOCIATION | ORGAN POLSKIEGO TOWARZYSTWA STOMATOLOGICZNEGO



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RECEIVED: 16.03.2019 • ACCEPTED: 02.07.2019 • PUBLISHED: 19.07.2019

INTRODUCTION

The frequency of salivary gland tumours remains high enough to date from 1% to 5% of all human tumours [14]. Among benign tumours, pleomorphic adenomas dominate from 61% to 90%, and among malignant tumors, adenocarcinomas – 20% [12]. The prevalence of various morphological types of salivary gland tumors by age and gender in different regions of the world (Europe, China, the countries of the Caribbean, South America, and Africa) is approximately the same [4, 11, 16, 18].

Most of the tumours of the salivary glands in the early stages have no pronounced typical clinical symptoms, which leads to late appearance of patients to the doctor. Methods of diagnosis and treatment of these diseases are sufficiently known (computed tomography [CT], magnetic resonance imaging [MRI], ultrasound [US], sialography, and partial, subtotal, total parotidectomy, etc.) [7]. Despite the constant improvement of diagnostic methods, errors at the clinical stage of setting the provisional diagnosis remain rather high. Also, there are significant differences between the clinical and pathohistological diagnosis – 30-40% [8].

The pleomorphic adenoma remains one of the most common tumours of the salivary glands. The final diagnosis of “pleomorphic adenoma” is established on the basis of a pathohistological study. Morphological methods not only indicate the type of tumour – benign or malignant, but also determine its origin (phenotype of the tumour).

To date, in accessible sources of literature there are several morphological classifications of pleomorphic adenomas, which emphasise their origin [5]. However, despite a large number of works devoted to the study of various issues of the prevalence, aetiology, clinic, diagnosis, and treatment of patients with pleomorphic adenoma of the salivary glands, the number of morphological works devoted to this topic, in which the histological types of structure reflected on a sufficient statistical number of patients, and their distribution by age and gender, are practically absent.

OBJECTIVES

The purpose of our research was to make an analysis of archive materials of patients with neoplasms of the salivary glands that were treated at the department of O.O. Bogomolets NMU in the last five years.

MATERIAL AND METHODS

The material for the survey were archival histories of 232 patients with neoplasms of the salivary glands, who were treated at the Kyiv City Clinical Hospital No. 12 on the clinical base of the department of O. O. Bo-

gomolets NMU in the period 2014-2018. The average age of patients was 50.0 ± 15.3 years. Women totalled 151 (65.09%) and men 81 (34.91%). All patients underwent general clinical examinations (blood tests, electrocardiography, CT, MRI, US, etc.). All patients were given a typical surgical intervention – excisional biopsy, partial, subtotal, total parotidectomy. Postoperative material passed the necessary pathohistological study. For the processing of statistical data, Statistica and Excel software (OS Windows 7) was used. In the developed age-groups, male and female comparisons (mesenchymal and epithelial, mesenchymal and classical [combined], epithelial and classical [combined] histological types of pleomorphic adenomas) were defined as the average arithmetic mean, standard deviation, standard error of arithmetic mean, Student’s criterion, and *p*-value.

RESULTS

The frequency of different types of salivary gland neoplasms were analysed by the date of pathohistological examination in the period 2014-2018 (*n* = 232) (Table 1).

In total, for the period 2014-2018, 232 patients with a diagnosis of salivary gland neoplasm were examined.

Among 232 patients, 133 (57.32%) had pleomorphic adenomas, 33 (14.22%) had adenolymphomas (Warthin tumour), 48 (20.68%) had carcinomas, and other pathological processes accounted for 3% or less – retention cyst with signs of inflammation, inflammatory granuloma, lymphoepithelial lesion and myoepithelial lesion of salivary glands, and oncocytoma.

The distribution of the number of patients by gender (2014-2018) was analysed with typical (most common) neoplasms of the salivary glands (pleomorphic adenomas, adenolymphomas [Warthin tumour], adenocarcinomas), where the percentage of patients was calculated for each group separately.

TABLE 1. The frequency of different types of salivary gland neoplasms by the date of pathohistological examination in the period 2014-2018 (*n* = 232)

Diagnosis	Absolute quantity	Relative quantity (%)
Pleomorphic adenoma	133	57.32
Adenolymphoma (Warthin tumour)	33	14.22
Carcinoma	48	20.68
Retention cyst with signs of inflammation	7	3.01
Myoepithelial lesion of salivary glands	6	2.58
Lymphoepithelial lesion	2	0.86
Inflammatory granuloma	2	0.86
Oncocytoma	1	0.43
Total number of patients	232	100

The analysis of data in Table 2 showed that most pleomorphic adenomas and adenocarcinomas occurred in women: 90 (67.67%) and 29 (60.42%), respectively; in men, by contrast, adenolymphomas (Warthin tumour) predominated – 24 (72.72%). By adenocarcinoma, in this article all malignant neoplasms of the salivary glands that occurred in the period 2014-2018 are noted.

Distribution of patients with neoplasms of the salivary glands depending on localisation of the tumour (parotid and submandibular gland, minor salivary glands) in the period 2014-2018 ($n = 232$) (Table 3).

The analysis of the distribution of patients with neoplasms of the salivary glands, depending on the localisation of the tumour (parotid and submandibular

TABLE 2. Distribution of the number of patients by gender (2014-2018) with typical (most common) neoplasms of the salivary glands (pleomorphic adenomas, adenolymphomas, adenocarcinomas), in which the percentage of patients was calculated for each group separately

Pleomorphic adenoma, $n = 133$		Adenolymphoma (Warthin tumour), $n = 33$		Adenocarcinoma, $n = 48$	
Men's	Women's	Men's	Women's	Men's	Women's
43	90	24	9	19	29
32, 33%	67, 67%	72, 72%	27, 28%	39, 58%	60, 42%

TABLE 3. Distribution of patients with neoplasms of the salivary glands depending on localisation of the tumour (parotid and submandibular gland, minor salivary glands) for 2014-2018 ($n = 232$)

Parotid salivary gland		Submandibular salivary gland		Small salivary gland	
Men's	Women's	Men's	Women's	Men's	Women's
*69 (35.2%)	*127 (64.8%)	*7 (29.16%)	*17 (70.84%)	*3 (25%)	*9 (75%)
**196 (84.48%)		**24 (10.35%)		**12 (5.17%)	

*Counting by gender (male-female) was conducted from the total number of patients with tumour-related tumours of the corresponding gland.

**Counting by gender (male-female) was conducted from the total number of patients with tumour defeat of all glands.

TABLE 4. Distribution of patients with neoplasms of the salivary glands for noncoincidence of clinical and pathohistological diagnosis for 2014-2018 ($n = 97$)

Clinical diagnosis	Pathohistological diagnosis	Number of patients
Pleomorphic adenoma	Types of adenocarcinomas	36 (37.11%)
Pleomorphic adenoma	Adenolymphoma (Warthin tumour)	23 (23.71%)
Pleomorphic adenoma	Inflammatory granuloma	2 (2.06%)
Pleomorphic adenoma	Lymphoepithelial lesion	1 (1.03%)
Pleomorphic adenoma	Myoepithelial lesion	4 (4.12%)
Pleomorphic adenoma	Retention cyst with signs of inflammation	5 (5.15%)
Fibroma	Pleomorphic adenoma	4 (4.12%)
Chronic lymphadenitis	Pleomorphic adenoma	(5.15%)
Retention cyst with signs of inflammation	Adenolymphoma (Warthin tumour)	2 (2.06%)
Adenolymphoma (Warthin tumour)	Retention cyst	1 (1.03%)
Lateral cyst of the neck	Adenolymphoma (Warthin tumour)	2 (2.06%)
Adenolymphoma (Warthin tumour)	Adenocarcinoma	1 (1.03%)
Adenolymphoma (Warthin tumour)	Lymphoepithelial lesion	1 (1.03%)
Pleomorphic adenoma	Lateral cyst of the neck (inflammation stage)	2 (2.06%)
Pleomorphic adenoma	Chronic lymphadenitis	2 (2.06%)
Pleomorphic adenoma	Oxyfilm adenoma	1 (1.03%)
Chronic lymphadenitis	Adenolymphoma (Warthin tumour)	1 (1.03%)
Tumour of submandibular area	Types of adenocarcinomas	2 (2.06%)
Tumour of submandibular area	Carcinoma in pleomorphic adenoma	1 (1.03%)
Tumour of submandibular area	Pleomorphic adenoma	1 (1.03%)

gland, minor salivary glands), indicates the prevalence of the pathological process in the area of the parotid salivary gland – 196 (84.48%) patients. By gender, women dominated in all types of glands.

Distribution of patients with neoplasms of the salivary glands for noncoincidence of clinical and pathohistological diagnosis during the period 2014-2018 ($n = 97$) (Table 4).

Thus, among 232 patients with neoplasms of the salivary glands in the period 2014-2018, in 97 (41.81%) there

TABLE 5. Distribution of patients by type of malignant neoplasm of the salivary glands for 2014-2018 ($n = 48$)

Diagnosis	Number of patients
Mucoepidermoid cancer	16 (33.33%)
Acinic-cellular adenocarcinoma	12 (25%)
Adenoid-cystic cancer	6 (12.5%)
Carcinoma in pleomorphic adenoma	7 (14.58%)
Basal cell adenoma	2 (4.16%)
Highly differentiated adenocarcinoma	1 (2.08%)
Epithelial-myoepithelial adenocarcinoma	1 (2.08%)
Malignant B-cell lymphoma	1 (2.08%)
Low-differentiated adenocarcinoma	1 (2.08%)
Neurogenic sarcoma	1 (2.08%)
Total number of patients	48 (100%)

TABLE 6. Distribution of patients with localisation of pleomorphic adenomas in the salivary glands for 2014-2018 ($n = 133$)

Type of salivary gland	Absolute quantity	Relative quantity
Parotid salivary gland	110	82.70%
Submandibular salivary gland	16	12.04%
Sublingual salivary gland	–	–
Small salivary glands	7	5.26%
Defeat of several salivary glands	–	–

TABLE 7. Distribution of patients (2014-2018) on different histological types of pleomorphic adenomas ($n = 133$)

Histological types of pleomorphic adenomas	Absolute quantity	Relative quantity
Mesenchymal	91	68.42%
Epithelial	30	22.56%
Classical (combined)	11	8.27%
Myoepithelial	1	0.75%
Total number of patients	133	100%

Counting the number of patients with different types of structure of pleomorphic adenomas was from the total number of patients with pleomorphic adenomas.

was no coincidence of clinical and pathohistological diagnoses. At the same time, in two groups of pathohistological diagnoses this percentage was the largest: (pleomorphic adenoma – carcinoma) – 36 (37.11%) and (pleomorphic adenoma – adenolymphoma [Warthin tumour]) – 23 (23.71%).

Distribution of patients by types of malignant neoplasms of the salivary glands for 2014-2018 ($n = 48$) (Table 5).

The analysis of data on the distribution of patients by type of malignant tumours of the salivary glands showed that the largest number of patients was those with mucoepidermoid cancer and acinic cell adenocarcinoma, in 16 (33.33%) and 12 (25%) patients, respectively.

Distribution of patients with localisation of pleomorphic adenomas in the salivary glands for 2014-2018 ($n = 133$) (Table 6).

The analysis of the distribution of patients by localisation of pleomorphic adenomas in the salivary glands for 2014-2018 indicates the prevalence of patients with lesions of parotid salivary glands – 110 (82.7%).

To calculate the distribution of patients with different types of pleomorphic adenomas by the histological structure, the classification proposed by Hus'kova [9] was taken into account. Thus, according to the classification, there are four types of pleomorphic adenomas by histological structure: mesenchymal, epithelial, classical (combined), and myoepithelial.

Distribution of patients (2014-2018) regarding different histological types of pleomorphic adenomas ($n = 133$) (Table 7).

The analysis of archival histories of patients with different types of pleomorphic adenomas by histological structure showed that the majority were patients with mesenchymal type of structure of pleomorphic adenoma – 91 (68.42%), with predominance of the epithelial component – 30 (22.56%), classical (combined), variant (the same number of mesenchymal and epithelial components) – 11 (8.27%), and with predominance of the myoepithelial component – 1 (0.75%).

Distribution of patients (2014-2018) regarding different histological types of pleomorphic adenomas by gender and age (Table 8).

The distribution of patients by gender among the main histological types of pleomorphic adenoma was as follows: women and men were dominated by mesenchymal and epithelial types of the structure of pleomorphic adenomas and comprised 64 (71.11%), 20 (22.22%), 27 (62.79%), and 10 (23.26%), respectively, and approximately an equal number of patients was with classical (combined) type – 5 (5.56%) and 6 (13.95%). The myoepithelial type of the structure of pleomorphic adenoma was met in only one case – 1 (1.11%) and was characteristic for female gender.

The distribution of age-related women and men among the main histological types of pleomorphic adenoma was as follows: the mesenchymal and classical (combined) type in both groups of patients (men and

TABLE 8. Distribution of patients (2014-2018) on different histological types of pleomorphic adenomas by gender and age

The histological types of the structure of the pleomorphic adenomas	Gender		Age	
	Men's	Women's	Men's	Women's
With domination of the mesenchymal component	**27 (62.79%)	**64 (71.11%)	41.29 ± 13.04 ($p < 0.05$)	43.84 ± 16.19 ($p > 0.05$)
With domination of the epithelial component	**10 (23.26%)	**20 (22.22%)	48.5 ± 11.66 ($p < 0.05$)	39.87 ± 9.74 ($p > 0.05$)
Classic (combined) variant (the same number of mesenchymal and epithelial components)**	**6 (13.95%)	**5 (5.56%)	43.2 ± 18.11 ($p > 0.05$)	45.42 ± 19.78 ($p > 0.05$)
With the domination of myoepithelial component**	–	**1 (1.11%)		
Total number of patients by gender**	**43	**90		

It should be noted that the calculation of patients with different types of histological structure of pleomorphic adenoma by gender was the result of the total number of patients belonging to this article.

women) was seen at approximately the same average age: 43.84 ± 16.19 and 45.42 ± 19.78 and 41.29 ± 13.04 and 43.2 ± 18.11 , respectively, there were significant differences for the epithelial type – women had an average age of 39.87 ± 9.74 years, and for men – 48.5 ± 11.66 years. The analysis of the results of the study showed that from the three groups of comparison (mesenchymal and epithelial, mesenchymal and classical (combined), epithelial and classical (combined) histological types of pleomorphic adenomas) among men and women by age, only in one group among men (mesenchymal and epithelial histological types of pleomorphic adenomas) are the calculated values of Student's criteria more critical, and therefore it is statistically reliable (significance level $p < 0.05$).

DISCUSSION

The salivary glands play an important role in the human body, performing secretory, excretory, endocrine, immune, and many other functions necessary for homeostasis. The variety of vital functions of the salivary glands makes them a dangerous target for the development of various pathological processes, including tumours. One of the risk factors for salivary gland tumours is chronic inflammation, caused by various types of viruses (paramyxovirus, cytomegalovirus) [10]. One of the most famous viruses that causes carcinogenesis is human papillomavirus (of 6, 11, 16, and 18 types). It was for the discovery of its participation in the development of cervical cancer that Harald zur Hausen received the Nobel Prize in physiology and medicine in 2008 [3]. Among the major benign tumours, the most common are pleomorphic adenomas and adenolymphomas (Warthin tumour), and among malignant – adenocarcinomas.

The analysis of the data showed that pleomorphic adenoma (57.32%) remains the most prevalent tumour of the salivary glands, which in the vast majority of patients (84.48%) is located in the parotid salivary gland and (67.67%) is found among female subjects. As can be

seen from the analysis of the archival data, the frequency of pleomorphic adenomas decreased in comparison with the statistics of the majority of foreign sources (according to EM Osipian, 2011; YH Matiakin 2010), the frequency of pleomorphic adenomas was 61-90% [13]. In turn, the domination of women in this neoplasm indicates a possible endocrine dependence of the tumour, namely the presence of oestrogen beta receptors in tumour tissues [19]. Unlike women, for men the tumours of the salivary glands were dominated by adenolymphomas (Warthin tumour), at 72.27%, which coincides with the data of most literary sources, in which the gender ratio (male : female) is between 3 : 1 and 5 : 1. The main reason for the dominance of the male article is a higher percentage of smokers among them because tobacco use is one of the main risk factors for adenolymphomas (Warthin tumour) [6].

The features of tumours of major salivary glands include an asymptomatic or low symptomatic course in the early stages, especially malignant, the complexity of differential diagnosis, a significant percentage of errors in diagnosis at the prehospital phase, late stage when seeking medical advice, and a significant recurrence rate. All of these factors require the maxillofacial surgeons to have sufficient knowledge and skills to carry out operative interventions and further prognosis for the disease.

Causes of errors in the diagnosis of tumours of the salivary glands include the following: insufficient qualifications of the doctor (carrying out only one of the necessary additional examinations – US, if necessary, at least two CTs + US, or MRI + US), unsatisfactory socio-economic status of the country, which in most cases prevents financially unstable patients from conducting additional examinations (CT or MRI of the salivary glands), and difficult anatomy of the minor salivary glands (the presence of a dense fascial-muscle layer in the area of the parotid salivary gland, distorting the palpation sense of density and consistency of the tumour, the presence of additional deep fragments of the glands, the location of major vessels and nerves).

Data analysis of the department of O.O. Bogomolts NMU for the period 2014-2018 showed that among 232 patients with neoplasms of the salivary glands, in 97 (41.81%) differences were observed in clinical and pathohistological diagnoses. The main group for this indicator is a pleomorphic adenoma – carcinoma (37.11%). Among the malignant tumours of the salivary glands, the greatest number of patients had mucoepidermoid cancer (33.33%). These data prove once again that in the early stages of the development of the tumour of the salivary glands, the type of tumour (malignant or benign) is difficult to detect, even using modern, advanced methods of examination (CT, MRI, US, FNAB, etc.).

Thus, one of the potential promising directions in the diagnosis and differential diagnosis of tumours of the salivary glands is the use and implementation of genetic technologies – the detection of genetic markers of tumours in different biological environments – blood, saliva, puncture of the tumour, and others.

Modern methods of diagnosis of salivary gland neoplasms, including pleomorphic adenoma, involve the study of the tumour not only at the stage of clinical examination (prehospital) but also after surgical intervention by the type of excision biopsy. Among the main methods of the final study of the removed tumour material are pathohistological and immunohistochemical approaches. Both of these examinations complement each other, ensuring the establishment of the most likely final diagnosis [2].

In our opinion, it is important to determine the types of histological structure (phenotype) of pleomorphic adenomas of the salivary glands, which will allow, in the future, prediction of the tendency of one or another type to degenerate (malignancy).

There are several known morphological classifications of pleomorphic adenomas. So, in particular, Hus'kova [9] distinguishes four histological types: mesenchymal, epithelial, classical (combined – equal number of mesenchymal and epithelial components), and myoepithelial [9]. Other authors [1] point to the existence of two types of histological differentiation of pleomorphic adenomas – mesenchymal and epithelial [1]. Triantafyllou *et al.* 2014 indicate the existence of three types: mesenchymal, epithelial, and its modification – myoepithelial [17]. Also, there is still discussion among researchers about which of the types (phenotypes) of histological structure of the pleomorphic adenoma is true – mesenchymal or epithelial, and whether it is possible to attach pleomorphic adenoma to mixed tumours, taking into account its multicomponent nature by types of histological structure.

Our analysis of 133 histories of diseases of patients with pleomorphic adenomas determined that in 110 patients the process was localised in the parotid salivary gland. The analysis of the types of histological structure (based on the classification of Hus'kova [9]) showed that in most patients mesenchymal and epithelial types

of pleomorphic adenomas predominate – 91 (68.42%) and 30 (22.56%) patients, respectively. The distribution by gender (male-female) also indicates the dominance of the mesenchymal and epithelial types of pleomorphic adenomas – 64 (71.11%), 20 (22.22%), 27 (62.79%), and 10 (23.26%), respectively. Significant differences in the age range were observed for epithelial type of pleomorphic adenomas: in women the average age was 39.87 ± 9.74 years, for men it was 48.5 ± 11.66 years.

The dominance of mesenchymal and epithelial histological types of pleomorphic adenomas statistically coincides with most foreign sources [14], and the predominance of the mesenchymal type confirms its major role in the formation of pleomorphic adenoma. The epithelial type of pleomorphic adenoma, in our opinion, is more prone to malignancy because it is the myoepithelium of the inserted ducts, which is on the basement membrane of the epithelial layer, which is one of the criteria for the transformation of a benign tumour into malignant.

CONCLUSIONS

In this article we discussed most of the statistics associated with salivary gland neoplasms, such as frequency of salivary gland tumours (benign and malignant), distribution of patients by gender and age, localisation of pathological process, non-coincidence of clinical and pathological diagnoses, histological types of pleomorphic adenomas, and their distribution depending on age and gender. For the practical doctor, non-coincidence between clinical and pathological diagnoses requires the introduction of new methods of examination of salivary gland tumours.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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