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Original Article

Clinicopathological Analysis of Ameloblastoma in a Northwestern Libyan Population: A 21-Year Retrospective Study

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ABSTRACT

Objectives. *The purpose of this study was to evaluate the prevalence and clinicopathological characteristics of ameloblastoma in a Northwestern Libyan population.* ***Methods.*** *A 21-year retrospective study of ameloblastoma cases histopathologically diagnosed at Tripoli University Hospital, Tripoli, Libya, archived from 2002 to 2022. Basic clinicopathological data, including age at diagnosis, gender, anatomical tumor location, and histopathological diagnosis, were collected and analyzed retrospectively. The diagnosis was based on the criteria of the latest updating fifth edition of the 2022 WHO classification of Head and Neck Tumors. The collected data were analyzed by IBM SPSS Statistics for Windows version 26.0.* ***Results.*** *Ameloblastoma tumors constituted 2.3% of all 2308 registered orofacial biopsy specimens. A total of 44 cases of ameloblastoma tumors were analyzed. Of these, 30 (68.2%), 12 (27.3%), and 2 (4.5%) cases were of conventional, unicystic, and peripheral types, respectively. Regarding gender, 54.5% of cases occurred in males; the male-to-female ratio was 1.2:1. The most frequent anatomical location was the mandible (81.8%), with a mandible-to-maxilla ratio of 6:1. The majority of cases were diagnosed as a painless swelling (80%). A wide age range (15 to 78 years) was recorded, with the mean age of all patients at diagnosis was 36.6 ± 16.2 years. The peak incidence was in the fifth and third decades of life. Follicular ameloblastoma was the most common histopathological subtype (29.3%), followed by plexiform ameloblastoma (25.0%). No statistically significant associations were found between types/subtypes of ameloblastoma tumors with regard to gender and age group distribution ($p > 0.05$).* ***Conclusion****. The profile of the ameloblastoma tumors included in this Northwestern Libyan sample was similar to the profile described for most other worldwide populations. The collected data in this study provides baseline data on types of ameloblastoma tumors, which is of significance to the oral pathologist and maxillofacial surgeon.*

Keywords: *Odontogenic Tumors, Ameloblastoma, Northwestern Libya, Retrospective*

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INTRODUCTION

Ameloblastoma is a benign, locally invasive epithelial tumor of the jaws with a strong tendency for recurrence if not removed adequately. Although rare, it is one of the most common odontogenic tumors [1].

According to the latest updated fifth edition of the World Health Organization (WHO) classification of Head and Neck Tumors published in 2022 [2], there are five types of ameloblastoma: conventional, unicystic, extraosseous/peripheral, metastasizing (malignant), and adenoid ameloblastoma. Based on this classification, histopathological subtypes

of conventional ameloblastoma include follicular, plexiform, acanthomatous, granular cell, basaloid, and desmoplastic patterns. Unicystic ameloblastoma is described as having three histopathological variants: luminal, intraluminal, and mural.

Conventional ameloblastoma is the most common type, usually diagnosed between the third and sixth decades of life with no gender predilection, and occurs most frequently in the posterior region of the mandible [1,3]. The biological behavior of conventional ameloblastoma is considered aggressive compared to other types due to its highest tendency to recurrence [1]. Moreover, it has been recommended that the mural variant of unicystic ameloblastoma should be treated as the conventional type [4].

Improper diagnosis and treatment of ameloblastoma may lead to recurrence, malignancy, and morbidity. Therefore, appropriate classification of tumors and accurate knowledge about the clinical characteristics and histopathological subtypes are essential for adequate management [5].

In Tripoli (the capital city of Libya and the city with the largest population), the Department of Pathology at Tripoli University Hospital (previously known as Tripoli Medical Center) serves as the main pathology diagnostic center, which receives almost all orofacial biopsy specimens from the Northwestern region of Libya.

Despite numerous studies that have evaluated the prevalence and frequency of ameloblastoma in various parts of the world, racial and geographic variations have been recognized, particularly in relation to demographic features and histopathological subtypes [3,6,7]. Since there is a lack of information in the English-language literature about the clinicopathological characteristics of ameloblastoma in a Northwestern Libyan population, we retrospectively reviewed ameloblastoma tumors over the last 21 years.

The purpose of the current study was to evaluate the prevalence, clinical, and histopathological features of ameloblastoma histopathologically diagnosed at Tripoli University Hospital, Tripoli, Libya, according to the 2022 WHO classification of Head and Neck Tumors in order to provide baseline data, which will be of significance to the oral pathologist and maxillofacial surgeon.

METHODS

Study Design and Sample

In this retrospective study, we reviewed the registry database of the Department of Pathology, Tripoli University Hospital, Tripoli, Libya, for all orofacial biopsy specimens archived during 21 years (from January 2002 to December 2022). Inclusion criteria were all histopathological reports with a diagnosis of ameloblastoma. Exclusion criteria were reports with incomplete clinical records, unavailability of histopathological slides, and non-Libyan nationality.

The hematoxylin and eosin (H&E) stained slides of all initially selected cases were retrieved and reviewed carefully by the authors in order to confirm the diagnosis for inclusion in the final sample. Then the confirmed cases were reclassified according to the criteria of the 2022 WHO classification of Head and Neck Tumors [2]. The histopathological subclassification of these tumors was based on the most predominant pattern, considering that a mixture of patterns was observed in a single lesion [8].

Information about gender, age at diagnosis, and anatomical tumor location of all histopathologically confirmed cases of ameloblastoma was obtained from the records of clinical data sent with the biopsy specimens.

Statistical Analysis

Statistical Product and Service Solutions (IBM SPSS Statistics for Windows, version 26.0; IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses of the collected clinicopathological data. Descriptive statistics were carried out; for quantitative variables, results were expressed as mean with standard deviation (SD), while qualitative variables were expressed as frequency and percentages. We used the chi-square test to analyze associations between qualitative variables (tumor type, gender, anatomical tumor location, age group, and histopathological subtypes). The level of statistical significance was set at a p-value < 0.05.

Ethical Consideration

Ethical approval to conduct this study was obtained from the Scientific Research and Ethics Committee at the University of Tripoli, Tripoli, Libya [reference number: SREC-UOT 03-2021]. The identities of the patients were kept anonymous, according to the World Medical Association Declaration of Helsinki.

RESULTS

During a 21-year period, a total of 2308 orofacial biopsy specimens were diagnosed at Tripoli University Hospital. Of these, 52 were diagnosed as ameloblastoma, accounting for 2.3% of all the registered lesions. However, eight cases were excluded from the current study due to incomplete clinical data acquisition or the unavailability of histopathological slides, leaving 44 cases that composed the final sample. Based on the 2022 WHO classification, our final sample (44 cases) of ameloblastoma tumors was divided into: 30 (68.2%) conventional, 12 (27.3%) unicystic, and only 2 (4.5%) cases of peripheral ameloblastoma (Figure 1). Neither a single case of metastasizing (malignant) nor adenoid ameloblastoma was documented.

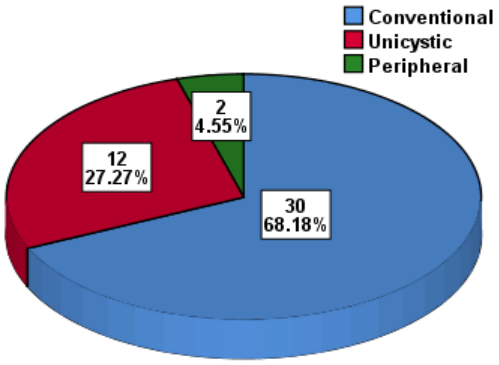

Figure 1. Frequency of types of ameloblastoma tumors.

Among all cases, 24 (54.5%) were male and 20 (45.5%) were female, with an overall male-to-female ratio of 1.2:1 (Figure 2). According to the chi-square test, there was no significant difference in gender distribution between different types of ameloblastoma (p = 0.074) (Table 1).

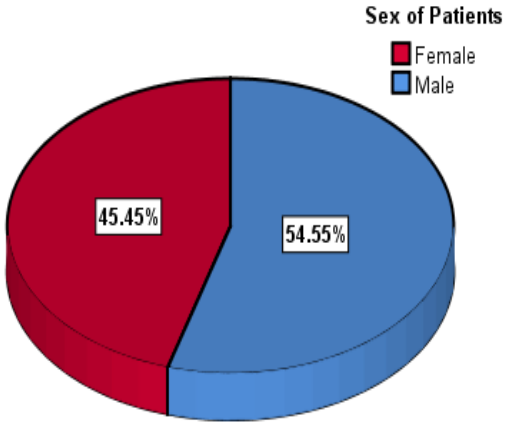

Figure 2. Gender distribution of ameloblastoma tumors.

Table 1. Gender distribution of ameloblastoma tumors.

Type of tumor	Total n (%)	Gender - n (%)	
		Male	Female
Conventional	30 (68.2)	13 (43.3)	17 (56.7)
Unicystic	12 (27.3)	9 (75.0)	3 (25.0)
Peripheral	2 (4.5)	2 (100)	0 (0)
Total n (%)	44 (100)	24 (54.5)	20 (45.5)
p-value	**0.074**		

Regarding the anatomical distribution of ameloblastoma, the predominant location was the mandible (36 cases; 81.8%), while the maxilla was affected in 6 (13.6%) cases, and 2 (4.5%) cases were located in soft tissue. Table 2 shows the anatomical distribution of ameloblastoma. In the mandible, the majority of cases occurred in the retro-molar area. The overall mandible-to-maxilla ratio was 6:1. Interestingly, the right side (19 cases; 43.2%) was more commonly affected than the left side (16 cases; 36.4%). Temporomandibular joint (TMJ) involvement was recorded in 2.3% (n = 1) of the cases. There was a statistically significant association between tumor types and their anatomical location ($p < 0.001$).

Table 2. Anatomical distribution of ameloblastoma tumors

Type of tumor	Total n (%)	Location - n (%)		
		Mandible	Maxilla	Soft tissue
Conventiona	*30 (68.2)*	*28 (93.3)*	*2 (6.7)*	*0 (0)*
Unicystic	*12 (27.3)*	*8 (66.7)*	*4 (33.3)*	*0 (0)*
Peripheral	*2 (4.5)*	*0 (0)*	*0 (0)*	*2 (100)*
Total n (%)	*44 (100)*	*36 (81.8)*	*6 (13.6)*	*2 (4.5)*
p-value	***< 0.001****			

* *Statistically significant*

In our sample, we observed that ameloblastoma occurred in the age range from 15 to 78 years at diagnosis, with the peak incidence in the fifth decade (12 cases; 27.3%), followed by the third decade (10 cases; 22.7%). The average age of all patients at diagnosis was 36.6 ± 16.2 years (mean = 36.6, SD = 16.2) and the mean age of patients with conventional, unicystic, and peripheral ameloblastoma was (37.0 years), (36.8 years), and (30.0 years), respectively. No statistically significant association was found between age group distribution and different types of ameloblastoma ($p = 0.815$) (Table 3).

Our findings indicated that the main complaint was painless swelling in the involved area (80%). Only one case reported an unhealing oral ulcer, accounting for 2.3% of the cases. Regional lymphadenopathy was noticed in 5 (11.4%) cases. The duration of symptoms varied from 8 months to 6 years.

Regarding the histopathological characteristics of conventional ameloblastoma, we observed that several cases had a mixture of histological patterns. However, the most common pattern encountered was follicular (13 cases; 43.3%), followed by plexiform (10 cases; 33.3%), desmoplastic (6 cases; 20.0%), and acanthomatous (1 case; 3.3%). Although a granular pattern was observed, it was not predominant in any case.

By considering the variants of unicystic ameloblastoma, the most common variant was the mural (7 cases; 58.3%), followed by luminal (4 cases; 33.3%), while intra-luminal was the least common variant (1 case; 8.3%). The peripheral ameloblastoma was characterized by the presence of plexiform (1 case; 50%) and acanthomatous (1 case; 50%) patterns.

Table 3: Age group distribution (decades of life) of ameloblastoma tumors.

Type of tumor	Total n (%)	Age group - n (%)						Mean age ± SD
		10-19	20-29	30-39	40-49	50-59	≥60	
Conventional	30 (68.2)	5 (16.7)	6 (20.0)	5 (16.7)	7 (23.3)	4 (13.3)	3 (10.0)	37.0 ± 15.5
Unicystic	12 (27.3)	2 (16.7)	4 (33.3)	0 (0)	4 (33.3)	1 (8.3)	1 (8.3)	36.8 ± 18.6
Peripheral	2 (4.5)	1 (50.0)	0 (0)	0 (0)	1 (50.0)	0 (0)	0 (0)	30.0 ± 18.4
Total n (%)	44 (100)	8 (18.2)	10 (22.7)	5 (11.4)	12 (27.3)	5 (11.4)	4 (9.1)	36.6 ± 16.2
p-value	**0.815**							

Among all histopathological subtypes, the most common subtype in this series was follicular ameloblastoma accounted for 13 (29.5%), followed by plexiform ameloblastoma accounted for 11 (25.0%), mural unicystic ameloblastoma accounted for 7 (15.9%), desmoplastic ameloblastoma accounted for 6 (13.6%), luminal unicystic ameloblastoma accounted for 4 (9.1%), and acanthomatous ameloblastoma accounted for 2 (4.5%), while intra-luminal unicystic ameloblastoma was the least common subtype, accounting for 1 (2.3%) (Figure 3).

Table 4 shows the gender and anatomical distribution of the total histopathological subtypes of ameloblastoma tumors. No statistically significant associations were observed between histopathological subtypes of ameloblastoma with regard to gender and age group distribution (p = 0.468; p = 0.379, respectively). However, there was a statistically significant association between the total histopathological subtypes of ameloblastoma tumors and their anatomical location (p = 0.027).

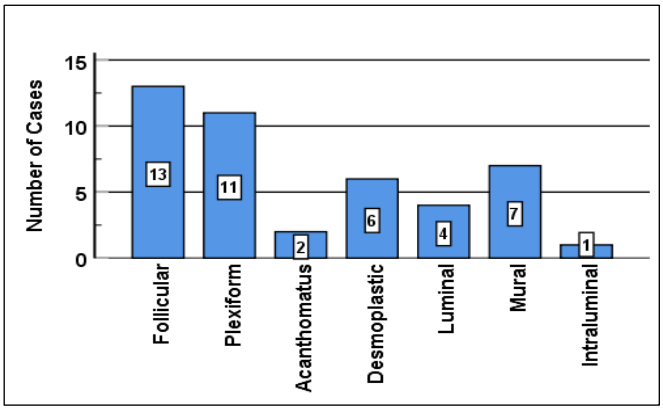

Figure 3. Frequency of the total histopathological subtypes of ameloblastoma tumors.

Table 4. Distribution of the total histopathological subtypes of ameloblastoma tumors according to gender and anatomical location.

Subtype of tumor	Total n (%)	Gender - n (%)		Location - n (%)		
		Male	Female	Mandible	Maxilla	Soft tissue
Follicular	13 (29.5)	5 (38.5)	8 (61.5)	13 (100)	0 (0)	0 (0)
Plexiform	11 (25.0)	6 (54.5)	5 (45.5)	10 (90.9)	0 (0)	1 (9.1)
Desmoplastic	6 (13.6)	3 (50)	3(50)	4 (66.7)	2 (33.3)	0 (0)
Acanthomatous	2 (4.5)	1 (50)	1 (50)	1 (50)	0 (0)	1 (50)
Mural unicystic	7 (15.9)	4 (57.1)	3 (42.9)	5 (71.4)	2 (28.6)	0 (0)
Luminal unicystic	4 (9.1)	4 (100)	0 (0)	2 (50)	2 (50)	0 (0)
Intra-luminal unicystic	1 (2.3)	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)
Total n (%)	44 (100)	24 (54.5)	20 (45.5)	36 (81.8)	6 (13.6)	2 (4.5)
p-value	**0.468**			**0.027***		

* *Statistically significant*

DISCUSSION

To our knowledge, four published studies were investigating ameloblastoma tumors among the Libyan population. A study was conducted by Hatem *et al*. [9], which analyzed the frequency of all benign orofacial lesions, including ameloblastoma at Tripoli University Hospital in Northwestern Libya. Similarly, there are three studies from Benghazi in Eastern Libya; two studies briefly discussed ameloblastoma while evaluating the frequency of benign tumors of the orofacial region at Arab Medical Science University [10], and odontogenic tumors at Benghazi University Teaching Hospital [11]. The third study by Elfergani *et al*. [12], evaluated the clinical and histopathological features of 28 cases of ameloblastoma in Benghazi. The current study is the first study dedicated to analyzing the clinicopathological characteristics of ameloblastoma in a Northwestern Libyan population, making the present study of great importance in providing precise information on the ameloblastoma profile in this geographic area.

Our results showed that ameloblastoma tumors accounted for only 2.3% of all registered orofacial biopsy specimens at Tripoli University Hospital during the past 21 years. This finding is in accordance with the results of Hatem *et al*. [9], EL-Gehani *et al.* [10], and Goteti [11], who reported that the prevalence of ameloblastoma tumors was 1.5%, 1.4%, and 3.6%, in the Northwest and Eastern regions of Libya, respectively. This result may indicate that ameloblastoma tumors are uncommon in the Libyan population.

Conventional ameloblastoma was the most common type in the present study (68.2%), followed by unicystic (27.3%), and peripheral (4.5%) ameloblastoma tumors. These findings are comparable to those reported in other studies [5,13–17]. On the other hand, Ledesma-Montes *et al*. [18] from Latin American populations and Elfergani *et al*. [12] from Eastern Libya reported that unicystic ameloblastoma was the most common type. These diverse findings among different populations may suggest the possibility of racial and geographic variations.

A slight male predilection was observed in our sample with a male-to-female ratio of 1.2:1, which is consistent with reports by Hendra *et al*. [7], Krishnapillai and Angadi [8], Filizzola *et al*. [13], Giraddi *et al*. [19], Intapa [20], and Aregbesola *et al*. (21). In contrast, a previous study from Tripoli University Hospital by Hatem et al. [9] reported a female predominance. This discrepancy might be attributed to sample size, and indeed, the present study had a larger sample than the previous study.

According to present data, the posterior region of the mandible was the most preferred site for ameloblastoma (81.8%), followed by the maxilla (13.6%), which is in line with other studies from the literature [13–16,18,22,23]. On the other hand, the anterior region of the jaw was observed to be the most common site in blacks [3] and the Nigerian population [24].

In our series, the mandible-to-maxilla ratio was 6:1. A similar distribution was recorded by Reichart *et al*. [3] in their review of the biological profile of 3677 cases of ameloblastoma in the literature, where they found that the ratio was 5:1.

The occurrence of ameloblastoma more predominantly on the right side of the jaws (43.2%) is comparable to the 48.4% reported by Giraddi *et al*. [19]. However, this finding is in contrast to other studies [8,25,26], where dominance was on the left side. This observation suggests the almost unilateral involvement of the jaws. TMJ involvement recorded in the present sample is in accordance with the results of a study conducted by Krishnapillai and Angadi [8].

Although a wide age range (15 to 78 years) was observed in the present study, we found that ameloblastoma occurred more often in the third and fifth decades of life. These results are in line with the global incidence of ameloblastoma, according to the review by Hendra *et al*. [7] who found that the worldwide peak incidence was in the third decade of life. Also, they reported that the peak incidence in Europe and North America, Africa and South

America, and Asia was in (the fifth & sixth decades), (the third decade) and (between the third & sixth decades), respectively.

In the current study, the mean age at diagnosis was 36.6 years. This finding is consistent with an extensive review by Reichart *et al*. [3], which found that the average age at diagnosis was 35.9 years.

Our observation was that the main complaint was painless swelling, which is considerably similar to other reports in the literature [3,8,17,18,22,25]. Traditionally, most Libyan citizens do not undergo regular dental check-ups under normal circumstances. This is possibly the reason why painless lesions are rarely detected early until the tumors have reached huge sizes.

Unhealing oral ulceration and regional lymphadenopathy were observed in our sample, which is in accordance with previous studies [3,8,12,14,18,27]. Oral ulceration is a rare clinical manifestation of ameloblastoma that might indicate the indolent growth of the tumor [8,28].

Regarding all histopathological subtypes, follicular ameloblastoma was the most common subtype in this study, which is in agreement with other studies [6,7,13,23–27]. However, previous studies by EL-Gehani *et al*. [10], Saghravanian *et al*. [5], and Intapa [20] reported that plexiform ameloblastoma was the most common histopathological subtype, followed by follicular ameloblastoma. On the other hand, Krishnapillai and Angadi [8] found that the most prevalent histopathological subtype was unicystic ameloblastoma. These diverse findings might be explained by the different methodologies used or the possibility of racial and geographic variations. Several studies [14,16,29] subclassified ameloblastoma when there was a mixture of two or more patterns into mixed ameloblastoma. Furthermore, Patsa *et al*. [16] reported that the presence of a mixed follicular and plexiform pattern without the predominance of any pattern could make it difficult to determine the exact subtype of ameloblastoma by an oral pathologist.

Consistent with our findings, several studies reported that there were no statistically significant associations between tumor types/subtypes and gender [5,13,29] or with age group distribution [13,29], whereas Saghravanian *et al*. [5] showed a statistically significant difference between tumor types and the mean age of patients.

The limitation of the present study is that the data were collected from a hospital-based database in a single institution, which is limited to demographic data and histopathological diagnosis of ameloblastoma. It lacks information related to radiographic features, follow-up, and recurrence. However, Tripoli is the capital city of Libya and the largest city by population, Tripoli University Hospital is considered the biggest teaching hospital in Libya with a bed capacity of more than 1200 beds, with the majority of cases from the Northwestern region of Libya. Hence, it remains a good option to select as a representative of the Northwestern population of Libya. Also, this study invaginated ameloblastoma tumors for 21 years, providing baseline data on these uncommon tumors.

CONCLUSION

According to our findings, ameloblastoma was uncommon in the Northwestern Libyan population. Conventional ameloblastoma was the most common type, with a slight male predominance. The principal anatomical location was the mandible, and follicular ameloblastoma was the most common histopathological subtype. The profile of ameloblastoma tumors included in this Northwestern Libyan sample was similar to the profile described in most other worldwide populations. The collected data in this study serves as baseline data on types of ameloblastoma tumors, which is of significance to the oral pathologist and maxillofacial surgeon.

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Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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