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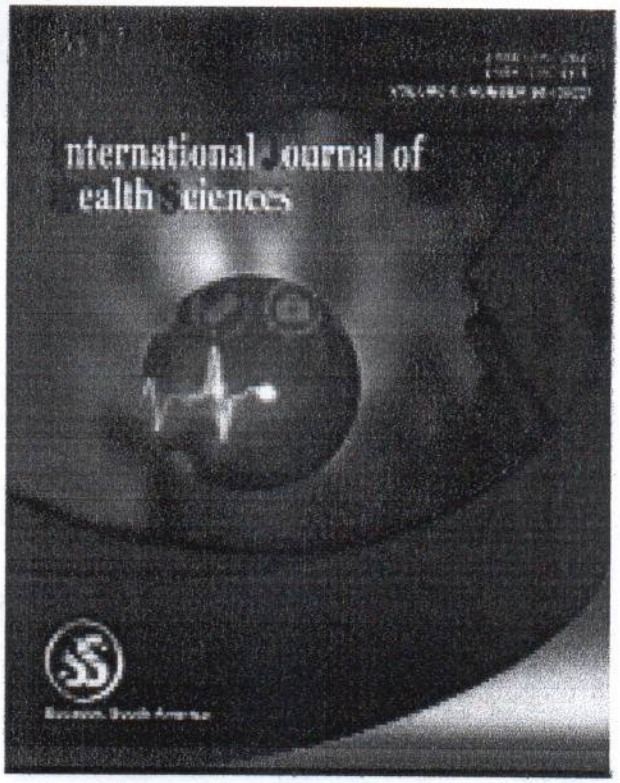
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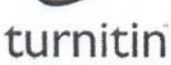

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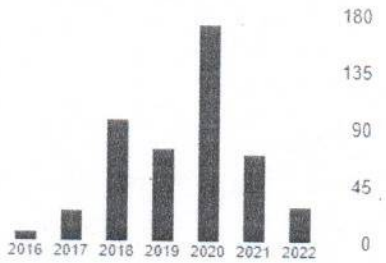

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Clinicopathological profile of ameloblastoma: A retrospective study for 5-years

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***Abstract*---**The emergence of ameloblastoma as the second most common odontogenic tumor that occurred after odontomas is a rare capacity to metastasize. Furthermore, this study aims to determine the clinicopathological profile of ameloblastoma. This was a descriptive retrospective study. The samples were obtained from histopathological examination data from the patients with ameloblastoma from January 2016 to December 2020 at the Anatomical Pathology Laboratory of Dr. Soetomo Academic General Hospital Surabaya. Moreover, the diagnosis of confirmed ameloblastoma was obtained in 95 cases. The occurrence age of ameloblastoma in both jaws ranged from 7-84 years with a mean age of 36.3 years. In this case, the highest number of patients with ameloblastoma has occurred in the 41-50 years age group with 21 cases (22%). There was no gender predilection in ameloblastoma. The most common location of ameloblastoma was found in the mandible which was confirmed in 82 cases (86%) and found in the maxilla for 13 cases (14%). In all, the most common type of ameloblastoma found was solid/multicystic ameloblastoma in 88 cases (93%) and unicystic ameloblastoma in 7 cases (7%). In the extent of solid or multicystic ameloblastoma, the most common mixed type was confirmed in 41 cases (43%) and the most diverse incidence being plexiform and follicular types. These data are expected to serve as baseline information on the occurrence of various histopathological types of ameloblastoma at the Anatomical Pathology Laboratory of Dr. Soetomo Academic General Hospital. Furthermore, these are expected as a basis for future epidemiological data as well.

***Keywords*---**Ameloblastoma, Clinicopathology, Histopathological type.

Introduction

Ameloblastoma is categorized as a benign epithelial odontogenic tumor that grows progressively. It is characterized as an expansion and a tendency for local recurrence as if it is mistreated. As a result, it leads to facial disfigurement and functional problems (Cadavid *et al.*, 2019; Vered *et al.*, 2017). According to WHO (2017), ameloblastoma is a rare odontogenic tumor that has the estimated annual incidence is only about 0.5 cases per million population (Vered *et al.*, 2017). Hariram *et al* stated that ameloblastoma is confirmed in 1-3% of all tumors and cysts of the jaws (Hariram *et al.*, 2014). In fact, ameloblastoma is commonnly found in Asians and Africans than Latin Americans and Europeans (Siar *et al.*, 2012). There is no predilection for gender in ameloblastoma. The highest incidence of ameloblastoma is in the third and fourth decades, with a patient age range of 8-92 years (Cadavid *et al.*, 2019; Vered *et al.*, 2017).

WHO (2017) divides ameloblastoma into four variants that consist of solid or multicystic ameloblastoma, unicystic type ameloblastoma, extraosseous or peripheral type ameloblastoma, and metastasizing ameloblastoma (Vered *et al.*, 2017). Solid or multicystic ameloblastoma is more common than unicystic ameloblastoma. There are six histopathological subtypes of solid or multicystic ameloblastoma i.e. follicular, plexiform, acanthomatous, granular, basaloid, and desmoplastic. These subtypes can either be single or mixed (Vered *et al.*, 2017).

Based on the etiopathogenesis, ameloblastoma originates from the unerupted dental lamina and occurs through mutations in the *MAPK* (Mitogen-activated protein kinase) and *SMO* (Smoothened) gene pathways (Vered *et al.*, 2017; Hariram *et al.*, 2014). Furthermore, this retrospective study aims to describe the clinicopathological profile of ameloblastomas which were thoroughly diagnosed at the Anatomical Pathology Laboratory of Dr. Soetomo Academic General Hospital Surabaya for five years.

Materials and Methods

After obtaining permission from the Research Ethics Committee No. 1271/120/4/II/2022 at the Faculty of Medicine of Universitas Airlangga, a total of 95 cases from the histopathological examination were diagnosed as solid or multicystic ameloblastoma and unicystic ameloblastoma. These data were taken for detailed analysis at the Anatomical Pathology Laboratory of Dr. Soetomo Academic General Hospital Surabaya. In this study, the data reported from January 2016 to December 2020 were observed. The materials were analyzed by considering patients' gender, their age group, the location of ameloblastoma, the type of specimen, and the histopathological type of ameloblastoma. Moreover, the hematoxylin and eosin stain sections were only used to diagnose all cases.

Results and Discussions

A total of 95 cases from the histopathological examination were diagnosed as solid or multicystic ameloblastoma and unicystic ameloblastoma. These data were taken for detailed analysis at the Anatomical Pathology Laboratory of Dr. Soetomo Academic General Hospital Surabaya.

Gender distribution

A total of the 95 cases were consisted of 48 male (49%) and 47 female patients (51%). There was no gender predilection (Table 1).

Age group distribution

The distribution of the age group of 95 cases of ameloblastoma consisted of the followings criteria; 1-10 years age group were occurred in two cases (2 %), 11-20 years age group were occurred in 16 cases (17 %), 21-30 years age group were occurred in 19 cases (20 %), 31-40 years age group were found in 19 cases (20%), 41-50 years age group were confirmed in 21 cases (22 %), 51-60 years age group were confirmed in 13 cases (14 %), 61-70 years age group were confirmed in three cases (3 %), 71-80 years age group were confirmed in one case (1 %), and 81-90 years age group were found in one case (1 %). The most age group distribution was found in the 41-50 years age group with 21cases (22%). The age of occurrence of ameloblastoma in both jaws ranged from 7 to 84 years with a mean age of 36.3 years (Table 1).

Tumor location

The location of ameloblastoma is in the mandible and maxilla. The most common site of ameloblastoma was originated from the mandible that found in 82 cases (86%) and from the maxilla that found in 13 cases (14%) (Table 1).

Table 1
Distribution patient of ameloblastoma (gender, age distribution and tumor location)

Patient Characteristic	n	%
Gender		
Males	48	49 %
Females	47	51 %
Age		
1-10	2	2 %
11-20	16	17 %
21-30	19	20 %
31-40	19	20 %
41-50	21	22 %
51-60	13	14 %
61-70	3	3 %
71-80	1	1 %
81-90	1	1 %
Tumor location		
Mandibula	82	86 %
Maxilla	13	14 %

Histopathological type

Among histopathological types, solid or multicystic ameloblastoma was the most common type with 88 cases (93%) compared to unicystic ameloblastoma in seven cases (7%). In the extent of solid or multicystic ameloblastoma, the mixed type was occurred in 41 cases (43%) and the plexiform type with 23 cases (24%), follicular type was found in 17 cases (18%), acanthomatous type with five cases (5%), granular type with one case (1%) and desmoplastic type with one case (1%) as well (Table 2). In this study, the findings were depicted as the followings; the most occurrences were plexiform as found in 41 cases of the mixed type, the follicular types were occurred in 31 cases, followed by five cases of mixed follicular and acanthomatous type, two cases of mixed plexiform and acanthomatous type, two cases of mixed plexiform, follicular and acanthomatous type and a case of plexiform, follicular, acanthomatous and basaloid type. Furthermore, the microscopic features from ameloblastoma can be seen in Figure 1 and Figure 2.

Table 2
Histopathological type

Age group	Solid or Multicystic Ameloblastoma						Unicystic Ameloblastoma
	Follicular	Plexiform	Acanthomatous	Granular	Desmoplastic	Mixed	
1-10	0	1	1	0	0	0	0
11-20	1	8	1	0	0	3	3
21-30	0	3	1	1	1	10	4
31-40	1	7	1	0	0	11	0
41-50	9	2	0	0	0	9	0
51-60	5	1	0	0	0	7	0
61-70	1	1	1	0	0	0	0
71-80	0	0	0	0	0	1	0
81-90	0	0	0	0	0	1	0
Total	17	23	5	1	1	41	7

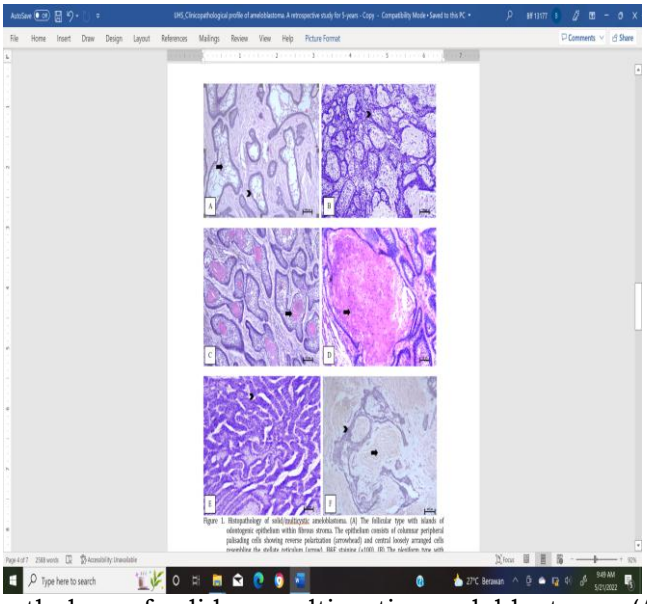

Figure 1. Histopathology of solid or multicystic ameloblastoma. (A) The follicular type with islands of odontogenic epithelium within fibrous stroma.

The epithelium consisted of columnar peripheral palisading cells showing reverse polarization (arrowhead) and central loosely arranged cells resembling the stellate reticulum (arrow). H&E staining (×100). (B) The plexiform type with anastomosing strands and cord of basal cells (arrow), delicate stroma, and inconspicuouss stellate reticulum. H&E staining (×100). (C) The acanthomatous type featured squamous metaplasia in the stellatereticulum-like central areas (arrow). H&E staining (×100). (D) The granular type showed granular change in stellate reticulum-like central areas (arrow). H&E staining (×100). (E) The basaloid type with epithelium consisted of basaloid peripheral palisading cells (arrowhead). H&E staining (×100). (F) desmoplastic ameloblastoma consisted of cuboidal to flat peripheral cells (arrowhead) with densely collagenous stroma (arrow). H&E staining (×100).

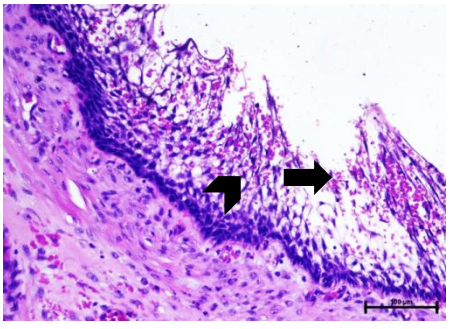

Figure 2. Unicystic ameloblastoma showed a simple cyst and lined by characteristic ameloblastomatous epithelium with peripheral palisading and

nuclear polarization (arrowhead), overlying loosely arranged cells that may resembles stellate reticulum (arrow)

As a matter of fact, ameloblastoma is a benign epithelial odontogenic neoplasm. Furthermore, solid or multicystic ameloblastoma is a benign intraosseus that grows progressively as epithelial odontogenic neoplasm. It is characterized by expansion and tendency for local recurrence as if it is not adequately removed. Unicystic ameloblastoma is a variant of intraosseous ameloblastoma that occurs in cystic cavity with or without luminal proliferation (Vered *et al.*, 2017). In this study, the distribution of ameloblastoma cases based on age found that the most common age group was in the 41-50 years with 21 cases (22%). Moreover, this incidence rate was in accordance with the statement of WHO (2017) that the most common age is in the fourth and fifth decades (Vered *et al.*, 2017). Hendra *et al* stated that the incidence of ameloblastoma cases in Asians occurred between the third decades while the worldwide rate occurred in the third decade. The incidence in Africa and South America was commonly to be found at a younger age i.e. in the third decade; however, the incidence in Europe and North America was commonly to be found at the older age i.e. the fifth and final decades (Hendra *et al.*, 2019)

The mean age of the patients in the time of initial diagnosis was 36.3 years. This notion was in accordance with the research of Hresko *et al* and Milman *et al* in getting the average incidence of ameloblastoma at the age of 36 years (Hresko *et al.*, 2021; Milman *et al.*, 2016). In this study, the cases of ameloblastoma within the age ranged from 7 to 84 years was in accordance with WHO (2017) where the age range of ameloblastoma incidence is 8 to 92 years. Furthermore, Cadavid *et al* found that ameloblastoma was commonly occurred in the age range of 9 – 82 years (Cadavid *et al.*, 2019; Vered *et al.*, 2017).

Secondly, the distribution of ameloblastoma cases based on sex groups i.e. 48 cases (51%) occurred in male patients and as many as 47 cases (49%) in female patients. There was no gender predilection in this study. This was in accordance with WHO (2017), Cadavid *et al* and Intapa in the extent of the research to obtain that there was no ameloblastoma in gender predilection (Cadavid *et al.*, 2019; Vered *et al.*, 2017; Intapa, 2017). Hendra *et al* stated that the incidence of ameloblastoma in Asia, Africa and North America was predominantly male; however, it is not statistically significant (Cadavid *et al.*, 2019; Hendra *et al.*, 2019; Intapa, 2017).

The most frequent cases of ameloblastoma located in the mandible were 82 cases (86%) compared to those which were found in the maxilla as 13 cases (14%). This result was in accordance with WHO (2017) and Neville *et al* that 80%-85% cases of ameloblastoma occur in the mandible while 15-20% in the maxilla (Neville *et al.*, 2016; Vered *et al.*, 2017). Hendra *et al* stated that the incidence rate in the mandible was more often as many as 87.2% and in the maxilla as many as 8.5% (Hendra *et al.*, 2019). Patsa *et al* found that the incidence of ameloblastoma in the mandible was 85.13% more frequent while in the maxilla was 14.87% (Patsa *et al.*, 2016). Khatri *et al.* Thus, ameloblastoma in the mandible was 85.2% more than in the maxilla which was 14.8% (Khatri *et al.,* 2015).

Based on the pathogenesis, the location of the ameloblastoma can be defined by gene mutations. Ameloblastoma in the mandible is more common with *BRAF* mutations as many as 72%. Nevertheless, mutations in the *RAS* family, *FGFR2* and *SMO* are very rare with a proportion of 5% each. Ameloblastoma in the maxilla is more common with mutations in the *SMO* (50%), *RAS* (40%), *BRAF* (20%) or *FGFR2* (15%) genes (Evangelou *et* al., 2020; Vered *et al.*, 2017).

Cadavid *et al* stated that the cases of solid/multicystic ameloblastoma was the most frequent among other histopathological type with an incidence rate of 85% cases (Cadavid *et al.*, 2019). This was in accordance with our study which found more cases of solid or multicystic ameloblastoma as many as 88 cases (93%) compared to unicystic ameloblastoma in seven cases (13%). Solid or multicystic ameloblastoma consisted of follicular type, plexiform type, granular type, basaloid type and desmoplastic type. The most common ameloblastoma occurred in the Anatomical Pathology Laboratory, RSUD Dr. Soetomo was the mixed type which was 41 cases (43%) and the rare case was granular type in one case (1%) and desmoplastic type was in one case (1%) as well. The most cases of mixed type ameloblastoma were plexiform and follicular type as many as 31 cases. This notion was in accordance with the study of Patsa *et al.* that described the type of ameloblastoma i.e. a mixture of plexiform and follicular types (Patsa *et al.*, 2016). Moreover, according to WHO (2017) and Hendra *et al*, ameloblastoma can occur in a mixed (Vered *et al.*, 2017). In this study, unicystic ameloblatoma consisted of four cases (57%) in 21-30 years age group and three cases (43%) in 11-20 years age group. This result was coherent with the statement of WHO (2017). It stated that approximately 50% of cases are diagnosed in the second decades of life with a patient's age ranges from 1-79 years (Vered *et al.*, 2017).

Conclusion

A total of 95 cases were diagnosed as ameloblastoma which occurred in the most age group of 41-50 years. Moreover, ameloblastoma was found the most in the mandible. In this study, there was no gender predilection. The most common histopathological type was mixed between plexiform and follicular types was found in 31 cases.

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