

A 30-year review of ameloblastoma: A tertiary hospital-based study

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ABSTRACT

Introduction

The clinical, histological and radiographic presentation of ameloblastoma is well described in the literature. This odontogenic tumour commonly affects the mandible and is locally aggressive and destructive, resulting in disfigurement. Ameloblastoma arises from dental tissues at various phases of tooth development. They are generally asymptomatic, slow growing, locally invasive and rarely malignant with a high recurrence rate. The demographic predilection of these tumours is high in Africans, male and aged 30 years and below.

Objective

To test the hypotheses that ameloblastomas were predominant in the mandible among black Africans, males and the young.

Study design

Retrospective review of ameloblastoma cases from 1991 to 2022.

Methods

Data analysis was based on 185 histologically confirmed cases. Appropriate descriptive and inferential statistics were undertaken on age, gender, clinical, radiographic and histological characteristics.

Results

The average age was 28.81 (14.53), ranging between 3-75 years. The overall male to female ratio stood at 1.18:1. Ameloblastomas were prevalent in the mandible 174 (94.1%), diagnosed as conventional variant 155 (83.7%) and acanthomatous subtype. Radiographically, the lesions appeared as multilocular 97 (55.4%), radiolucent 100

(54.05%) and expansile 129 (67.7%). The average size of the lesions was 77.43 ± 33.83 mm, with a range of 184mm.

Conclusion

Our results validate the hypothesis that ameloblastoma is highly prevalent among black Africans of younger age. The radiographic, clinical and histological characteristics of ameloblastoma in our population are comparable to the vast literature.

Keywords

Ameloblastoma, multilocular, radiolucent

INTRODUCTION

Ameloblastoma is a benign tumour arising from dental tissues at various phases of tooth development.¹⁻⁴ Though rare, this tumour constitutes between 1% and 11% of all head and neck and odontogenic tumours respectively.¹ Ameloblastomas are generally asymptomatic, slow growing, locally invasive and rarely malignant; however, they exhibit high recurrence rates.⁵ Unless diagnosed early, ameloblastoma can cause considerable disfigurement in affected patients.^{2,6}

According to the World Health Organization's new classification of ameloblastoma, lesions are classified as benign and malignant. The benign variants include (i) unicystic ameloblastomas which are subclassified as luminal, intraluminal and/or mural, (ii) conventional ameloblastoma and (iii) peripheral ameloblastoma. Malignant lesions are classified as (i) ameloblastic carcinoma and (ii) metastasising ameloblastoma, a somewhat controversial lesion also termed "malignant ameloblastoma".

Ameloblastomas have distinct diagnostic features which were documented by Vickers and Gorlin in 1970.⁷ These include the presence of peripheral palisaded columnar cells which have hyperchromatic nuclei exhibiting reverse nuclear polarisation and infranuclear vacuolation. Several histological variants have been described for the conventional form of ameloblastoma based on unique histological characteristics. These histological variants have no prognostic significance; however, the knowledge of their diversity may facilitate histological diagnosis.⁵⁻⁸

The distinction between the unicystic and conventional forms of ameloblastoma is of clinical significance which dictates the degree of surgical intervention. Unicystic ameloblastomas are most often diagnosed in the second decade of life with substantive literary evidence which supports a more conservative surgical approach for the luminal and intraluminal subtypes which may avoid aggressive resections at an age at which facial development and tooth eruption is still actively occurring.

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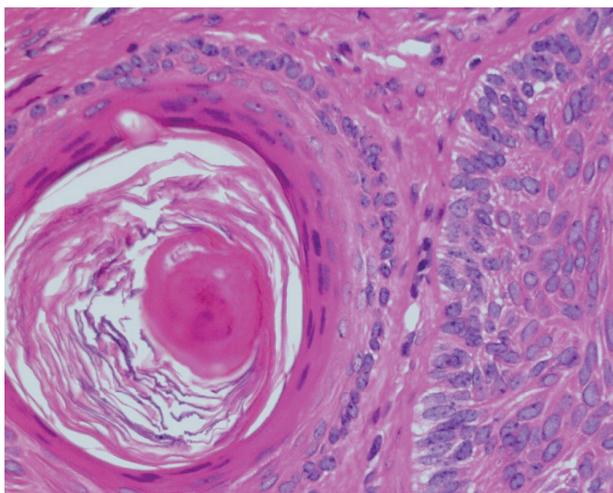


Figure 1: Acanthomatous variant, displaying how with this variant the central islands and stellate-like reticulum cells undergo squamous differentiation resembling squamous epithelium. (Haematoxylin and Eosin stained.)

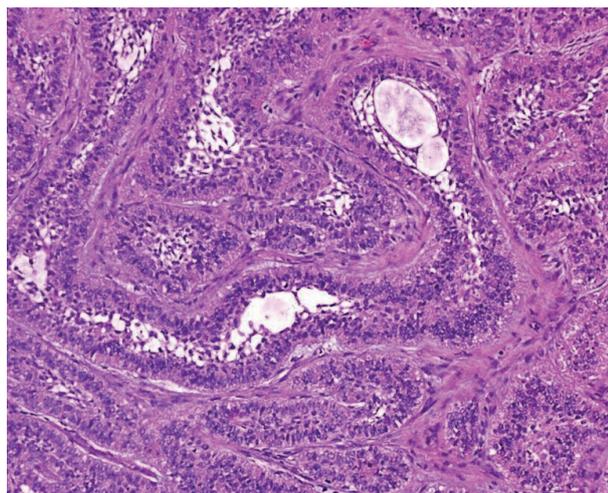


Figure 2: Haematoxylin and Eosin stain specimens showing plexiform ameloblastoma.

Conventional ameloblastoma is the most frequently diagnosed variant, affecting patients aged between 30 and 40 years.⁶⁻⁹ This variant is more aggressive, highly recurrent and requires radical surgical management than other subtypes.^{10,11} There are an array of histological subtypes for conventional ameloblastomas, none of which has proven to be of prognostic significance; however, knowledge of this histological diversity facilitates accurate diagnosis. The malignant forms of ameloblastoma will be surgically treated as for any form of malignant odontogenic neoplasm. The varied radiographic characteristics of ameloblastomas demonstrate differences in biological behaviour and can be of prognostic significance.⁷⁻¹⁰ Radiographic features of prognostic importance include locularity, site and size of lesions, as well as the effects on the surrounding structures.

Lesions with ill-defined borders, cortical expansion and breakthrough often require radical surgical intervention and increase the risk of tumour recurrence.^{10,12,13} There are marked clinico-demographic distributions of ameloblastoma globally. Systematic reviews and meta-analyses indicate significant patterns with regard to gender, age and site of lesions. Males are affected slightly more than females (M:F ratio = 1.14:1; $p < 0.001$); the peak incidence is at 30 years, and 90% of tumours are located within the mandible.^{1,3,11-14}

The aim and clinical significance of this second largest South African study in recent times was to test the hypotheses that ameloblastomas were (i) predominant among black Africans, (ii) have male gender predilection, (iii) affected mainly young age groups, and (iv) occurred mostly in the mandible, and were large in size.

MATERIALS AND METHODS

Study design

A retrospective study was undertaken at the Sefako Makgatho Health Sciences University (SMU) to review ameloblastoma cases from 1991 to 2022.

Study population

The study population included all available records of patients diagnosed with ameloblastoma, and eligible for inclusion in this study based on the following criteria:

- (i) Complete and accurate patient records (demographic details; histological reports; panoramic radiographs)

- (ii) Panoramic radiographs of good diagnostic quality (cases with radiographic deterioration were excluded on the basis that they could invalidate the data collection)

Sampling and sample size

No sampling or sample size determination was undertaken for this study. It was anticipated that more than 120 records would be included in our study, which is more than most cases reported in the literature.^{10,13,15}

Data collection

A specially designed data collection tool was developed to assess the following variables: (i) demographics (age and gender), (ii) clinical information, (iii) site and radiographic features, and (iv) histological characteristics.

MEASUREMENT OF VARIABLES

Clinical information

Clinical information included the main complaint and symptoms. For consistency, the following symptoms were recorded as swelling, pain, local discomfort, infection (purulent discharge), paraesthesia, delayed healing of extraction socket and tooth mobility.

Site

The site of the tumour was categorised into the following regions of the mandible: (i) anterior (incisal-canine), (ii) body (premolar-molar), (iii) posterior (distal to third molar), and (iv) bilateral regions (across the midline). Specific anatomical landmarks were recorded: the posterior which included the ramus, angle, coronoid process and condyle. In the maxilla, the tumour was sited as extending to the maxillary sinus and approaching the zygomatic arch and orbital floor. Any tumour involving two or more sites was assigned to the region approximating the centre of the lesion.

Radiographic features

Radiodensity was classified as either radiolucent, radiodense or mixed (radiolucent and radiodense). The bony margins immediately adjacent to the lesion were described as well-defined or ill-defined. Lesions were radiolucent, either unilocular (when only one compartment was present) or multilocular (when numerous adjacent compartments were present (Figures 3 and 4). Further radiographic depiction followed Worth's description of ameloblastoma.



Figure 3: Panoramic radiograph of multilocular appearance on the left mandible area extending to the coronoid. This radiograph displays the soap bubble radiographic appearance of the entity coupled with an expansion of the cortical bone.

Accordingly, the multilocular lesions were described as being either soap bubble, honeycomb or spiderlike in appearance. If the lesion did not resemble any of these descriptions, it was recorded as "other". Signs of root resorption and/or tooth displacement were also recorded. The size of the lesions was measured in millimeters with a 150mm (6") electronic digital vernier caliper or the VUE PACS software across its widest length, between opposite borders. The panoramic radiographs were taken on a Gendex GX, Sirona ORTHOPHOSXG3 or a Kodak-Trophy K8000E (the manufacturer's specifications of magnification are between 1.25 and 1.27).

In order to standardise the settings for interpretation, all analogue radiographs examined in this study were observed on a bright and evenly illuminated light-reflecting radiograph viewing box within an enclosed room with no light entry. The digital radiographs were observed on a standardised

monitor in an enclosed room with no light entry using the VUE PACS Carestream software. The expansile nature of the lesion was noted by studying its effect on the cortex of the mandible and its effect on the sinuses in the maxilla.¹⁰

Histology

Unicyclic ameloblastomas can only be accurately subtyped histologically due to their shared radiological features. They comprise luminal, intraluminal and mural subtypes. The luminal and intraluminal subtypes are best treated by enucleation while tumours with any form of mural extension should be completely resected to prevent recurrence.

Histologically, conventional ameloblastoma will show the classical Vickers and Gorlin criteria;⁷ however, variable histological growth patterns have been described. These include lesions with plexiform growth, follicular growth, acanthomatous differentiation, basaloid features, granular

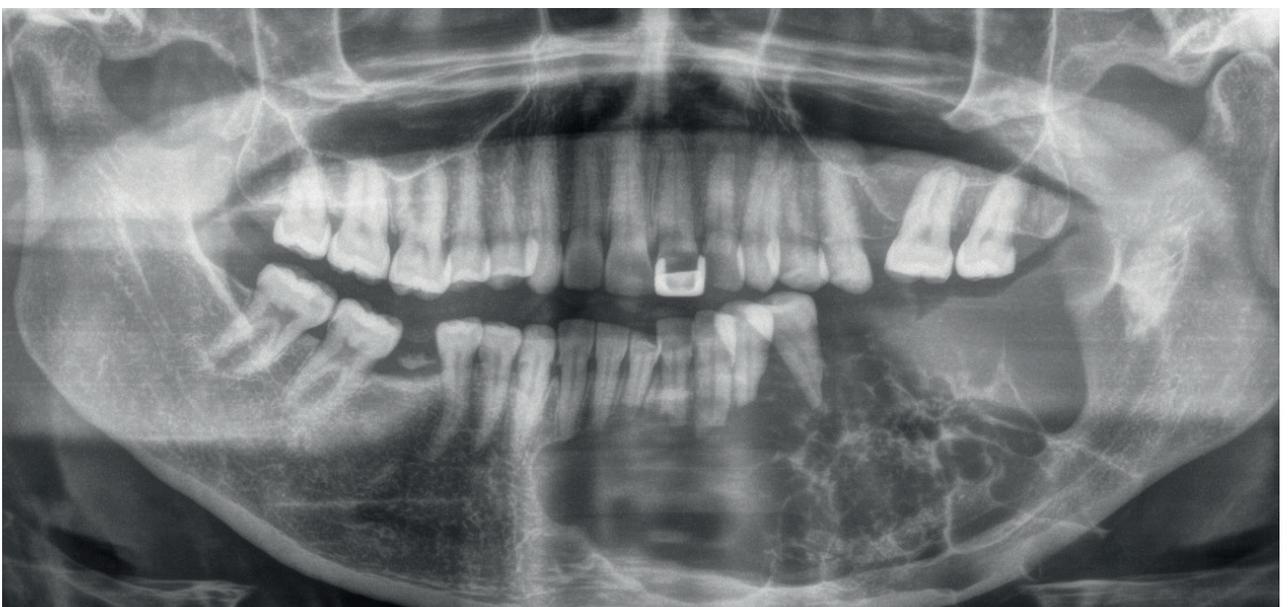


Figure 4: Panoramic radiograph of a multilocular lesion extending from the right to the left mandible. The lesion has resorbed and displaced the teeth in the mandible with a blunt appearance of the root apices. The lesion also displays a honeycomb appearance.

cell ameloblastoma, adenoid ameloblastoma and the desmoplastic subtype (Figures 1 and 2). The desmoplastic subtype of ameloblastoma was previously considered a separate form of ameloblastoma due to its unique clinicopathological and radiological features which are often indistinguishable from fibro-osseous lesions of the jaws.

The malignant variants of ameloblastoma include the ameloblastic carcinoma and the so-called “malignant ameloblastoma”. Ameloblastic carcinomas may arise de novo or may develop from a pre-existing benign conventional ameloblastoma. The typical ameloblastomatous features are abundantly clear; however, there is overt evidence of malignancy. The “malignant ameloblastoma” is a diagnosis which can only be made retrospectively. Patients will typically present with multiple tumour nodules in the lungs and will have a history of a previously resected conventional ameloblastoma. It is postulated that at the time of resection, friable fragments of tumour may inadvertently be aspirated and thus deposited in the lungs where they may continue to grow. The most significant feature of the malignant ameloblastoma is its banal, bland benign features which resemble those of the initial neoplasm which was previously resected.

In this study, the histological classification of ameloblastoma included the following types: unicystic, conventional, extraosseous peripheral metastasising (malignant), mixed or unspecified types. The subtypes comprised the following variants: acanthomatous (Figure 1), basal cell, follicular, granular cell, plexiform and combinations. The unspecified subtypes of ameloblastomas were excluded from the study.

STATISTICAL ANALYSIS

The statistical analysis was performed using IBM SPSS (Statistical Package for Social Sciences) version 28. Descriptive statistics included the measures of central tendency and dispersion (mean, standard deviation, and median and range) for numeric variables. Categorical variables were summarised using frequency and percentages. The Chi-square test and the Analysis of Variance (ANOVA) were computed to test for differences in the categorical and numeric variables between the two groups. Inferential analyses were performed at 5%.

Table 2: Distribution of ameloblastoma by site and gender

Site (Subtotal)	Gender n (%)		
	Male	Female	Total
Maxilla	5 (45.5)	6 (54.5)	11 (5.9)
Mandible	95 (54.6)	79 (45.4)	174 (94.1)
Body (symphysis, parasymphysis, angle)	58 (55.2)	47 (44.8)	105 (56.8)
Body and Ramus	19 (47.5)	21 (52.5)	40 (21.6)
Ramus, Condyle and Coronoid process	1 (33.3)	2 (66.7)	3 (1.6)
Body, Ramus, Condyle and Coronoid process	17 (65.4)	9 (34.6)	26 (14.1)
Total	100 (54.1)	85 (45.9)	185 (100)

Table 1: Age and gender distribution of ameloblastoma cases

Age (years)	Male	Female	n (%)	Ratio (M:F)
< 20	38	25	63 (34.1)	1.52:1
21 - 30	29	27	56 (30.3)	1.07:1
31 - 40	15	18	33 (17.8)	0.83:1
41 - 50	6	6	12 (6.5)	1:1
51 - 60	9	6	15 (8.1)	1.5:1
61 - 70	2	2	4 (2.2)	1:1
71+	1	1	2 (1.1)	1:1
Total	100 (54.1)	85 (45.9)	185 (100)	1.18:1

Ethical considerations

Ethical clearance to conduct this study was granted by Sefako Makgatho Health Sciences University Research and Ethics Committee SMUREC/D/112/2021: PG). The hospital manager and head of the department in the participating facility also granted permission to use the data. Participants' data were anonymised and kept confidential throughout the research process.

RESULTS

This 30-year retrospective review included 185 eligible cases of ameloblastoma. From 1991 to 2022, a total of 721 records were identified, of which 536 (74.3%) were excluded due to the following reasons: the definitive diagnosis of ameloblastoma could not be determined in three cases (3); degraded radiographs (22); duplicates (11) and missing biographical data (9). Most excluded records were due to illegible radiographic images – a total of 462 specimens did not have accompanying radiographs. These patients were referred from departments outside the SMU SOHS, which makes it difficult to access all the critical radiographic data. Eighteen accompanying radiographs were not panoramic but Lateral Obliques (2), Posterior Anterior view

Table 3: Radiographic features of ameloblastoma

Locularity	Radiodensity		
	Lucent	Mixed	Total
Multilocular			
Soap bubble	13	23	36
Honeycomb	1	8	9
Spiderlike	1	0	1
Other	13	38	51
Unilocular	72	16	88
Total	100	85	185

(3), Cone Beam Computer Tomography (10) and intra-oral radiographs (3). (The parenthesis indicates the number of radiographic images that were excluded in relation to the respective radiographic procedure.) We found that 11 images from the panoramic radiographs were beyond the focal trough; consequently, the dimensions of the lesion could not be measured and radiographic classification confirmed. Presented in table 1, are the demographic, radiographic and histological features of the 185 eligible cases of ameloblastoma.

Age and gender distribution of ameloblastoma

The average age of patients in this study was 28.81 years (14.53 Standard deviation), ranging from 3-75 years. The majority of ameloblastomas 152 (82.2%) were prevalent in patients 40 years and younger and were more common in males 100 (54.1%) than females 85 (45.9%). The overall male to female ratio stood at 1.18:1. A two-sided Fisher's exact test (FET) showed no association between age and gender ($p=0.869$).

Site distribution of ameloblastoma

Ameloblastoma was most prevalent in the mandible 174 (94.1%); of these males were more affected than females – 95 (54.6%) and 79 (45.4%) respectively. These differences in the site and gender distribution were not statistically significant ($p=0.575$). The maxilla accounted for 11 (5.9%) of the cases, which were approximately equally distributed among the genders (Table 2).

Histopathological features

The tumour classification showed the predominance of the conventional variant 155 (83.7%), with fewer of the unicystic and the-metastasising types, 29 (15.7%) and 1 (0.5%) respectively. Subtyping of 66 (35.7%) conventional ameloblastomas resulted in 36 acanthomatous, 15 plexiform, 10 follicular and 5 granular cell variants. This information was collected from archived histologic reports that were compiled and signed off by at least 2 oral pathologists using the diagnostic criteria that were considered the standard at the time. The histologic reports had additional information in the form of what additional cell type was present above and beyond the main ameloblastoma type; this information was then used to subtype into the different subtypes as described above.

Radiographic features

The majority of ameloblastomas were multilocular 97 (52.44%), radiolucent 100 (54.05%) and expansile 129

Table 4: Effect of ameloblastoma on surrounding structures

	Expansile		Total
	Yes	No	
Root resorption and displacement	91	27	118
Root/tooth displacement	18	16	34
Root resorption	8	6	14
No effect	0	1	1
No teeth	12	6	18
Total	129	56	185

(69.7%). More than one-third (36/97) of multilocular lesions exhibited a soap bubble appearance. Approximately 129 (69.73%) of ameloblastomas had effects on the adjacent structures which included root resorption 8 (4.32%) cases, displacement of teeth 18 cases (9.73%) and a combination of resorption and displacement 91 cases (49.20%). Only one case displayed no effect on adjacent dentition, while for 18 cases, there were no teeth adjacent to the lesion (Tables 3 and 4).

Size of ameloblastomas

The average size of the diagnosed lesions was 77.43 ± 33.83 mm, with a range of 184mm (3 – 187). Respective hypotheses evaluated the association of gender and age with the size of the lesion. ANOVA revealed that the mean size of ameloblastoma was greater in males (77.96 ± 33.28) mm than in females (76.82 ± 34.67) mm. However, this difference was not statistically significant ($p=0.82$). Similarly, the independent Kruskal – Wallis test showed no differences in lesion dimensions across the age groups ($p=0.93$). Compared to the maxilla, the mandibular lesions were dimensionally larger (mean 78.61mm versus 60.40mm); however, the differences were not significant ($p=0.071$). Statistically significant differences were found on the lesion dimensions and expansiveness (yes or no); effects on adjacent structures (yes or no) and locularity (multilocular vs unilocular). The associated statistical probabilities were $p<0.001$, 0.002 and $p<0.001$.

DISCUSSION

The purpose of this review was to gain a better understanding of the histological and radiographic characteristics of ameloblastoma in South Africa. There are four major findings of this study. First, ameloblastomas are most common in males under 30 years of age. Second, the condition occurs predominately in the mandible presenting as large expansile masses with cortical expansion with effects on adjacent structures. Third, on radiographic analysis ameloblastomas presented mainly as multilocular, radiolucent lesions with a soap bubble appearance. Fourth, histologically, most lesions represented conventional ameloblastomas of the acanthomatous subtype.

This large South African study directly demonstrates the demographic distribution of ameloblastoma. This demographic pattern is consistent with the published literature.¹⁶⁻¹⁹ According to the recent meta-analysis, the global gender distribution of ameloblastoma is estimated to be 1.14:1 (M:F). Continent-specific approximations were as

follows: Africa 1.20:1; North America 1.45:1; Asia 1.16:1 and Australia 1.73:1. These figures are comparable to our study results of 1.18:1 and 1.05:1, Ranchod *et al.*¹¹ However, the European and South American studies reported the predominance of ameloblastoma in women as compared to men with ratios of 1.14:1 and 1.25:1 respectively.¹⁴ This female gender predisposition confers no credible evidence or hypothesis for the female gender as a risk factor for the development of ameloblastoma; the same can be said in men as both genders are likely to exhibit the entity.

When comparing our results to those of Ranchod *et al.*¹¹, notably the age at which ameloblastoma is diagnosed has reduced over time, especially among African patients. The study of Ranchod *et al.* and this study support the hypothesis that the incidence of ameloblastoma is predominant in younger patients. Our study of 185 African patients yielded a mean age of 28.81 years, while in the Ranchod study 49 African patients contributed to a mean of 32.99 years.¹¹ These South African findings are congruent with studies that have confirmed the global peak incidence of ameloblastoma before the third decade among persons of African descent.^{14,19} It remains unclear to what degree the incidence of ameloblastoma at the age of 30 years or before is associated with African ancestry. It is, however, postulated that dire socioeconomic circumstances and inability to obtain adequate oral health treatment may render individuals more susceptible to the entity which can usually present itself at routine screenings or oral examinations. In these cases, lack of proper nutrition and limited access to appropriate medical care predispose Africans and South Americans to the early development of ameloblastomas. The association of genetic and socioenvironmental factors offers a plausible hypothesis for the development of ameloblastomas. However, this theory needs to be tested in well-controlled prospective longitudinal studies.

We found that the acanthomatous variant of conventional ameloblastoma was the most common histological subtype (54.54%). This is in contrast to the global data, which indicates that the most observed histological subtypes are follicular or plexiform variants.^{8,20} This finding is notable but inconsequential since it is well established that the histological subtypes do not have any meaningful effects on the treatment and prognosis. Multilocular ameloblastomas accounted for just over half of the lesions (52.44%) observed on Panoramic radiographs. This observation, though modestly lower, is consistent with what has been found in previous studies.^{11,21,22} On the contrary, unilocularity was significantly associated with younger age, $X^2(1,185) = 12.26, p < 0.001$. Based on the natural progression of the tumour, initial lesions are small and unilocular. However, as the tumour matures and expands it assumes a multilocular pattern. Ameloblastomas caused root resorption and displacement of teeth was observed in half of the subjects. This effect was conservative compared to Ranchod¹¹ Struthers²³ and Martins²⁴. Given the common effects of the tumour on the roots of teeth, ameloblastoma should be considered as part of any differential diagnosis where root resorption is present in young patients especially when there are no related symptoms. The mean size of ameloblastoma was 77.43mm, this result ties well with a local study by Ranchod *et al.*¹¹ (mean = 86.39mm). These data show that ameloblastomas in the South African population were highly expansile, affected adjacent structures and caused disfigurement. It is hypothesised that patients who wait longer without any medical intervention will present with large

neoplasms. The delays can be attributed to socioeconomic circumstances and inaccessible specialist oral health care services in these regions. Furthermore, malignant neoplasms are surgically prioritised while ameloblastoma, being benign, results in prolonged waiting times for surgical resection which often results in the development of massive lesions which then require extensive reconstruction and increase the risk of recurrence.

LIMITATIONS OF THE STUDY

A major concern is the exclusion of 536 cases, which underpowers the study, making it susceptible to random error. This methodological challenge can potentially invalidate the study results. However, our sample size is comparable to many published studies which could mitigate the minimal effect of random error and validate the study findings.

CONCLUSION

Our findings support the hypothesis that ameloblastoma is highly prevalent among black Africans of younger age. Furthermore, the lesions are highly expansile, larger in size and result in serious facial deformity. The radiographic, clinical and histological characteristics of ameloblastoma in our population are comparable to the vast literature.

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