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Original Article

Ameloblastoma of the mandible: analysis of radiographic and histopathological features

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Abstract – Introduction: Ameloblastoma is the most common benign tumour of odontogenic origin in Africa and presents five times more in the mandible than the maxilla. The presentation of ameloblastoma in the mandible is unique due to its anatomical variation and hence the aim of this study was to analyse the radiographic and histopathological features of ameloblastoma involving the mandible. **Materials and methods:** This was a retrospective, descriptive study of all histopathologically diagnosed ameloblastoma of the mandible over a period of 45 years. Patient demographics, radiographic and histopathological features were recorded and compared to previous studies. **Results:** A total of 148 lesions were included. The male to female ratio was nearly equal (1.05:1). The majority of patients were below 50 years of age (83.77%) and were black African (58.8%). The posterior region was the most affected site with majority of lesions presenting with multilocular appearance (68.24%) and root resorption (66.38%). Histologically, conventional ameloblastoma was the most common variant (48.65%). **Conclusions:** Mandibular ameloblastoma had a higher predilection for black African patients with higher prevalence of mixed density lesions when compared to previous studies. The size of lesions in this sample was considerably larger than those reported in previous studies. In addition, lesions in this sample also exhibited marked cortical expansion as well as root resorption.

Introduction

Ameloblastoma is the most commonly occurring benign tumour of odontogenic origin. It develops from epithelial cellular elements and dental tissue during their various phases of development. The prevalence of ameloblastoma in the mandible is approximately five times more than in the maxilla [1]. Its clinical presentation mimics that of an asymptomatic, slow-growing tumour, exhibiting a plethora of radiological and clinico-pathological features. Despite being benign in nature, ameloblastoma exhibits an invasive behavioural growth pattern, with a high rate of recurrence if not managed appropriately.

According to the World Health Organisation (WHO) ameloblastoma is known as the prototype of odontogenic tumours of epithelial origin [2]. The WHO further defines the ameloblastoma as a benign, slow-growing, locally invasive lesion of epithelial odontogenic neoplasm of putative enamel origin, and divides the lesion into three clinico-pathological types: conventional ameloblastoma (CA), unicystic ameloblastoma (UA), and peripheral ameloblastoma (PA) [2].

The literature has described a variation in the presentation of ameloblastoma in the maxilla as compared to the mandible [3,4]. The aim of this study was thus to evaluate the features of the ameloblastoma presenting in the mandible with emphasis on its radiographic and histopathological features and compare the findings to other studies.

Materials and methods

This was a retrospective, case-series, descriptive study of ameloblastoma of the mandible. This study followed the Declaration of Helsinki on medical protocol and ethics and the regional Ethical Review Board of the University of the Western Cape approved the study (approval number: BM/16/5/17). The study was a records review of patient demographic information, conventional radiographic presentation and histopathological features of ameloblastoma in the mandible for a 45-year period from 1972 to 2017.

Data collected included age, gender, ethnicity, radiographic and histopathological features. These features included size, location, radiodensity, bony margins, locularity, multilocular appearance, effect on adjacent dentition, and expansion of cortex.

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All pantomographs were examined by the same observer. The radiographic features of the lesion was examined according to established criteria and in cases of doubt, a second observer, an oral and maxillofacial radiologist, was consulted and a decision was reached by consensus.

The pantomographs used in this study were taken with either a GE-3000 (General Electric, Milaukkee, WI) or Cranex Tome CEPH (Soredex, Helsinki, Finland). In order to standardise the settings for interpretation, all radiographs were observed on a bright and evenly illuminated light-reflecting radiograph viewing box within an enclosed room with no light entry. Digital radiographs were observed on a standardised monitor in an enclosed room with no light entry. Magnifying glasses were used as adjunctive tools to allow for detailed examination of the radiographs when necessary.

The localization of the lesion was categorised according to five areas of the mandible. The first region was the anterior mandible which extended from the left canine to right canine, and in edentulous patients from the left to right mental foramina. The second was the posterior region of the mandible extending from canine to the angle of the mandible, for both left and right sides. The third region was defined as the ramus of the mandible, which extended from the angle of the mandible to the sigmoid notch. The fourth and fifth regions were represented by the extension of the lesion into the coronoid process or condylar head respectively.

Radiodensity was classified as either radiolucent, radiopaque or mixed (radiolucent and radiopaque). The bony margins immediately adjacent to the lesion were described as well-defined or unclear. Lesions were also classified as either unilocular (when only one compartment was present) or multilocular (when numerous adjacent compartments were present).

By referring to Worth's radiographic description (1963) [5] of ameloblastoma in the mandible, multilocular lesions were described as being either soap-bubble, honey-comb, or spider-like in appearance. If the lesion did not resemble any of these descriptions, it was noted as appearing as "other".

Signs of root resorption and/or tooth displacement illustrated the effect of the lesion on adjacent structures. The size of the lesion was measured in millimetres across its widest diameter, between opposite borders. The expansile nature of the lesion was noted by studying its effect on the cortex of the mandible.

Due to the changes in the classification between the 1972 and 2017 classification of lesions, information gathered regarding the specific histopathology was attained according to the conclusions provided.

The WHO 2017 classification of head and neck tumours, classified ameloblastoma as either conventional or unicystic types [2]. Some data reflected a diagnosis of ameloblastoma, but did not specify the type. These were classified as unspecified type.

Microsoft Excel was used to calculate and present the data. Data was analysed with StataCorp 2017 (Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC) in consultation with a statistician. Associations between categorical variables were tested by using the χ^2 test if assumptions were met. If the assumptions were not met, the *Fisher exact test* was used. For continuous data, an independent-samples t-test was run to determine if there were differences in the means between two groups. Furthermore, if more than two groups were present, a *One-way ANOVA* test was used to compare the differences between the means. The level of significance was set at $p < 0.05$.

Table I. Age and gender distribution of ameloblastoma within this sample.

Age group	No. patients	Percentage	No. males	No. females
10–19	29	19.59	10	19
20–29	48	32.43	25	23
30–39	25	16.89	14	11
40–49	22	14.86	18	8
50–59	13	8.78	7	6
60–69	7	4.73	4	3
70–79	3	2.04	2	1
80–89	1	0.68	0	1
Total	**148**	**100**	**76**	**72**

Results

A total of 209 patient records with a diagnosis of ameloblastoma were collected from the archives at the Department of Maxillo-Facial and Oral Surgery, Tygerberg Oral Health Centre. The records extended from 1972 to 2017. Seven cases with lesions found in the maxilla were excluded from the study. Of the remaining 202 cases, 148 had complete demographic information, radiographic evidence and a confirmed histopathological diagnosis.

Age

In this study, the ages of patients at time of diagnosis ranged from 11 to 83 years, with a mean age of 32.99 years. The majority of patients were under 50 years (83.77%) (Tab. I). Patients between the ages of 20 and 29 years were the most affected group (32.43%). Only one patient (0.68%) was in the 80 to 89 year group.

Gender

The male to female ratio was 1.05:1. There were 76 (51.3%) males and 72 (48.7%) females (Tab. I). The prevalence of ameloblastoma showed no statistically significant association between gender and age, as assessed by Fisher's exact test ($p = 0.503$).

Table II. Distribution of ameloblastoma in the mandible.

Location	No. of lesions	Percentage
Ameloblastoma involving one region		
Anterior	4	13.3
Posterior	26	86.7
	30	100
Ameloblastoma involving multiple regions		
Anterior and posterior	46	39
Anterior, posterior and ramus	2	1.7
Anterior, posterior, ramus and coronoid	4	3.5
Posterior and ramus	26	22
Posterior, ramus and coronoid	22	18.6
Posterior, ramus, coronoid and condyle	13	11.1
Ramus and coronoid	1	0.8
Ramus and condyle	1	0.8
Anterior, posterior, ramus, coronoid and condyle	3	2.5
	118	100

Ethnicity

Historically, South Africa had the following population racial groups: white, black, Indian and mixed race. This sample included patients from three ethnic groups. There were 87 patients (58.8%) in the black African group, 54 (36.5%) in the mixed race group and seven (4.7%) in the white group. There was no statistical significance in the prevalence of ameloblastoma among race and age categories as assessed by Fisher's exact test ($p = 0.852$).

Location

Thirty (20.3%) lesions involved only one region while one-hundred-and-eighteen (79.7%) extended across multiple regions (Tab. II). The majority of lesions involved anterior and posterior regions of the mandible 46 (39.0%) with fifty-one of these (34.46%) crossing the midline. None of the lesions were alone in the ramus, coronoid or condyle regions.

Radiodensity

Pantomographic examination revealed 76 lesions (51.35%) with radiolucent appearance while 71 (47.97%) had both radiolucent and radiopaque features (mixed density) (Fig. 1). Only one lesion (0.68%) had a unique radiopaque appearance and was unilocular in appearance.

Margins

One hundred-and-eighteen (79.73%) lesions presented with well-defined margins discernable from the surrounding unaffected bone compared to the 30 lesions (20.27%) which presented unclear margins.

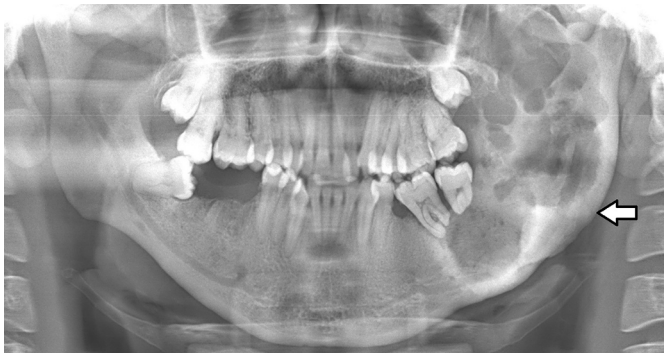

Fig. 1. Pantomograph showing both radiolucent and radiopaque appearance (mixed density) of an ameloblastoma in the left mandible.

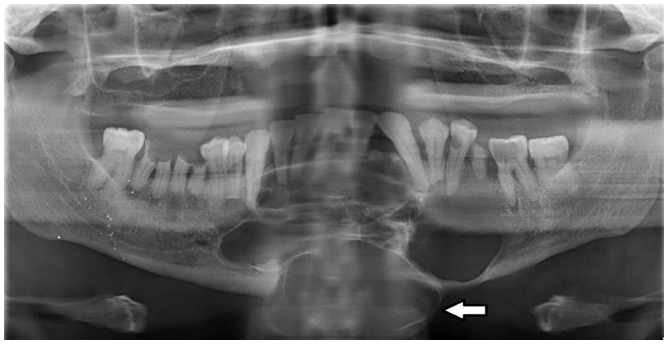

Fig. 2. Multilocular appearance of an ameloblastoma in the anterior and posterior regions of the mandible.

Locularity

Approximately two-thirds (68.24%) of lesions appeared as multilocular entities (Fig. 2), the remaining 47 (31.76%) appeared unilocular (Fig. 3). The majority of the multilocular

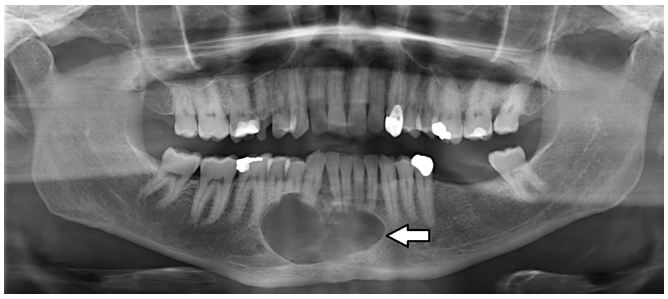

Fig. 3. Pantomograph showing unilocular ameloblastoma in the anterior mandible with signs of root resorption.

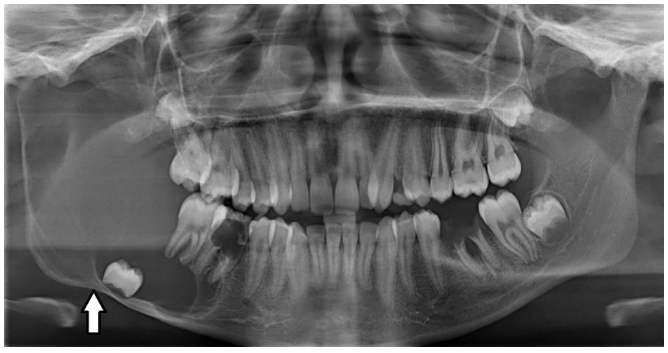

Fig. 4. Pantomograph showing multilocular, soap-bubble appearance of an ameloblastoma in the right mandible.

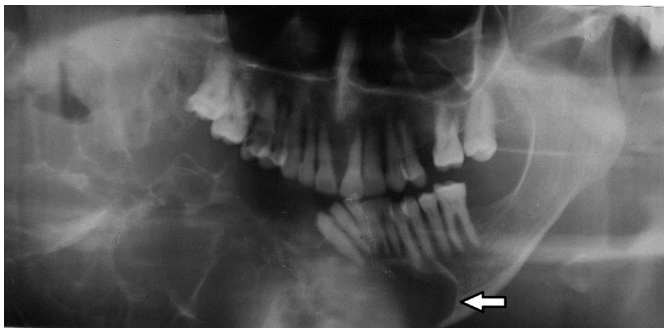

Fig. 5. Pantomograph showing multilocular lesion with a spider-like appearance of an ameloblastoma in the mandible.

Table III. Comparison of multilocular appearance and radiodensity on pantomograph.

Multilocular appearance	Radiodensity		Total
	Lucent	Mixed	
Spider-like	1	10	11
Honeycomb	3	13	16
Soap-bubble	37	32	69
Other	2	3	5
Total	**43**	**58**	**101**

variant (83.16%) observed, occurred in patients between the ages of 10 and 50 years. In contrast, 61.70% of the unilocular variant was observed in patients below the age of 30 years. There was however no statistically significant association between loculation and age as assessed by Fisher's exact test ($p = 0.391$).

Radiographic appearance

Approximately two-thirds (68.32%) of the lesions observed exhibited a soap-bubble appearance (Fig. 4). Sixteen lesions (15.84%) showed a honeycomb pattern, and 11 lesions (10.69%) appeared as spider-like (Fig. 5). The remaining five lesions (4.95%) did not look like any of the patterns stated above.

The majority of multilocular lesions in this study had a soap-bubble pattern and appeared as either lucent or of mixed density. According to the Fisher's exact test, this finding was statistically significant ($p = 0.004$) (Tab. III). Ameloblastoma caused expansion of the mandibular cortex in 103 patients (69.59%).

Effect of lesion on adjacent dentition

There was a comparative effect on the dentition in terms of root resorption (26.72%) and root/tooth displacement (27.59%). More than a third (39.66%) of all variants of ameloblastoma had the effect of both root resorption and root/tooth displacement. Only seven (6.03%) lesions did not have an effect on the adjacent dentition. In the remaining 32 cases (21.62%), there were no teeth next to the lesion or the jaws were completely edentulous.

When relating the effects of multilocular ameloblastoma on the dentition, there was no statistically significant difference ($P = 0.56$). The soap-bubble variant was however the most prevalent variant observed in this sample (Tab. IV).

Size of lesions

The size of the lesion was determined by measuring its largest diameter between opposite borders in millimetres (mm). The size ranged from 9 mm to 209 mm. The mean size was 86.39 mm. One-way ANOVA was conducted to determine whether the size of ameloblastoma differed among age groups. Data showed an even distribution for patient ages as assessed by the Shapiro-Wilk test ($p > 0.05$) (Fig. 6). The differences between these age groups was not statistically significant ($p = 0.1598$).

A one-way ANOVA was conducted to determine whether there was a difference in the size of the lesions among the three different ethnicities within the study. Ameloblastoma size in the black African group (mean 93.70 mm) was significantly larger when compared to the mixed race group (mean 75.98 mm) ($p = 0.018$).

Table IV. Multilocular pattern of ameloblastoma and its effects on dentition.

Multilocular pattern	Effect on dentition					Total
	Root resorption	Root/Tooth displacement	Resorption and displacement	No effect	No teeth	
Spider-like	2	3	5	0	1	11
Honeycomb	4	3	4	0	5	16
Soap-bubble	15	12	24	3	15	69
Other	0	3	0	0	2	5
Total	**21**	**21**	**33**	**3**	**23**	**101**

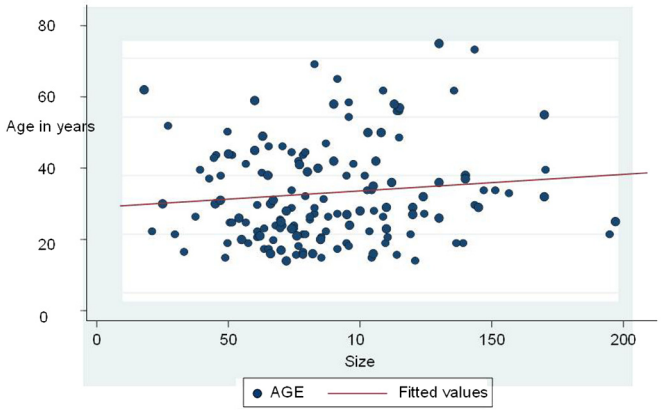

Fig. 6. Scatterplot of size versus age in patients with ameloblastoma.

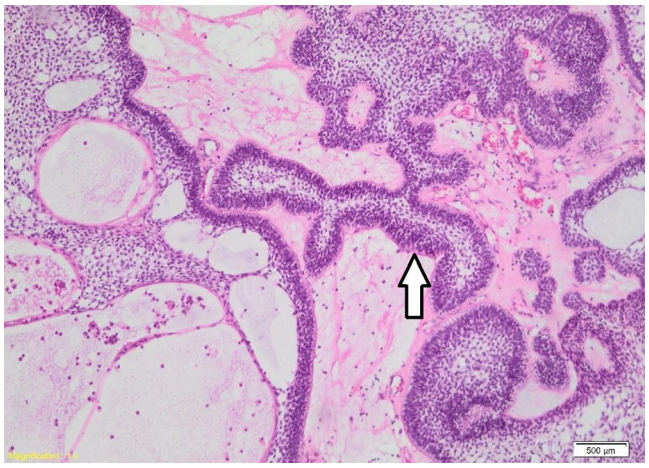

Fig. 7. H&E stained specimen showing plexiform ameloblastoma.

Histopathological features

A total of 72 specimen (48.65%) were diagnosed as conventional ameloblastoma using the WHO 2017 head and neck odontogenic tumour classification. The subtypes included 37 follicular, 12 plexiform (Fig. 7), three acanthomatous, two granular cell (Fig. 8) and two desmoplastic histopathological patterns. Radiographically, the majority of conventional ameloblastoma appeared as multilocular lesions (75.0%) and were of mixed density (54.2%).

Some histological patterns were observed to be combined within one lesion. Combinations of histopathological subtypes included: ten follicular-plexiform (Fig. 9), three follicular-plexiform-acanthomatous, two follicular-acanthomatous (Fig. 10) and one plexiform-acanthomatous.

Nineteen lesions (12.84%) were diagnosed as unicystic ameloblastoma (UA). The subtypes included: seven mural, two luminal, and two intraluminal. Eight tumours were classified as unspecified UA. The majority of unicystic ameloblastoma appeared as unilocular lesions on pantomographs (73.7%) and were radio-lucent (63.2%). Fifty-seven (38.51%) histopathological reports did not specify the type, but the diagnosis of ameloblastoma was confirmed.

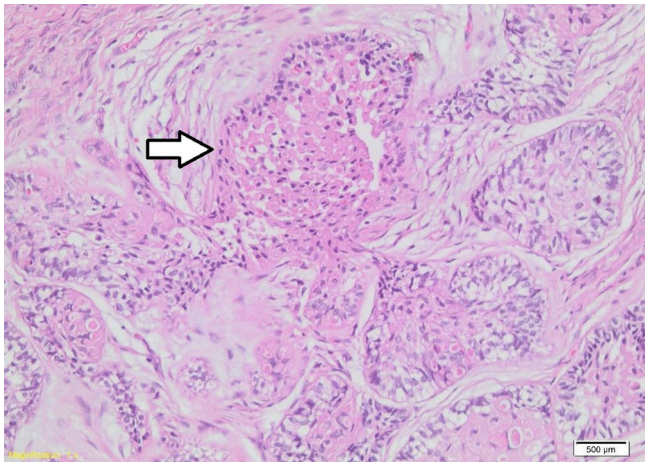

Fig. 8. H&E stained specimen showing follicular ameloblastoma with granular cell change.

Discussion

Mandibular ameloblastoma has unique radiographic and histopathological features most likely due to its distinct anatomical features. In this study we described a case-series of

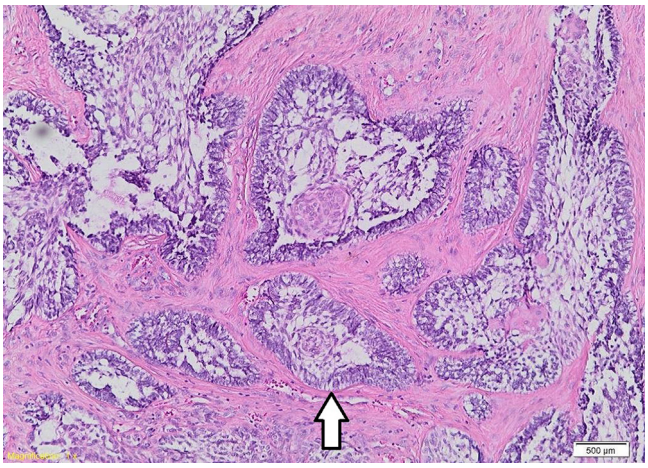

Fig. 9. H&E stained specimen showing follicular-plexiform ameloblastoma.

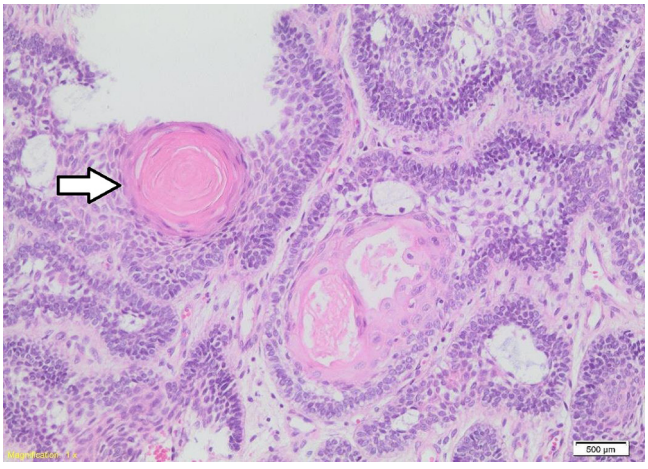

Fig. 10. H&E stained specimen showing follicular ameloblastoma with acanthomatous change.

ameloblastoma in a South African population group. To our knowledge, it is the largest cohort of mandibular ameloblastomas described in the literature.

The wide age range (11–83 years) presented in this study is comparable to other studies [1,6,7]. This age range is also described by MacDonald-Jankowski *et al.* [8] in a systematic review in 2004. The mean age of patients in this study was 32.99 years. Krishnapillai *et al.* [9], who conducted a study on an Indian population group, showed similar results. Furthermore, this result is supported by a large review of 2444 cases involving mandibular ameloblastomas by Reichardt *et al.* [1], which showed a mean age of 35.2 years old.

A nearly equal distribution between males and females was found in this study as well as in a study by Chukweneke *et al.* [10]. In contrast, a slight male predilection was shown in studies by Chawla *et al.* [11], Siar *et al.* [7] and More *et al.* [12], with ratios of male and female patients being 1.2:1, 1.4:1 and 1.2:1, respectively. Interestingly, this study demonstrated that ameloblastoma in the 5th decade of life had a predilection for males (18) compared to females (8). This could possibly be ascribed to the inherent culture of male patients in seeking professional medical assistance later in the disease process as compared to than their female counterparts [13].

More than half of all patients (58.8%) that presented with ameloblastoma of the mandible in this study were of black African descent. Even though black Africans constitute only 32.8% of the population in this region, this study showed that ameloblastoma occurred more often in black Africans but not significantly. Reviews by MacDonald-Jankowski *et al.* [8] and Reichardt *et al.* [1] also showed that this tumour had a predilection for black population groups. Oginni *et al.* [14] did not agree with this notion.

When comparing ameloblastoma in the maxilla to those in the mandible, numerous authors reported that maxillary lesions tend to occur more frequently in males with an average age of 54.9 years [3,15]. This is in contrast to mandibular lesions in this study which occurred nearly equally in males and females with a lower mean age of 32.99 years. Dyalram-Silverberg *et al.* [3] also demonstrated in their sample that maxillary lesions have a higher incidence in Caucasian patients as compared to mandibular lesions which occurred mostly in African American patients.

When assessing ameloblastoma of the mandible, radiographic modalities are useful in determining the size, extent, internal structure, margins and its effect on adjacent structures. With the introduction and use of advanced digital imaging, conventional radiography may appear out-dated. In rural settings or in the developing world this modality may still however be the mainstay of imaging either because advanced digital imaging is unavailable or simply too costly to implement. Pantomographs are still able to provide adequate information to assist in temporary diagnosis prior to histopathological confirmation.

Large reviews by Agbaje *et al.* [6], Ruslin *et al.* [16], Siar *et al.* [7] and Reichardt *et al.* [1] indicate that the mandibular posterior region is the most common site affected by ameloblastoma. The results from this study corroborate these findings. However, Chukweneke *et al.* [10] and Adekeye *et al.* [17] showed that the anterior region was more commonly involved. The difference in location in the various population groups is largely unknown and the histological and molecular characteristics of the tumour may be related to ethnic and geographic differences.

This study showed similar distribution of radiolucent, and mixed radiolucent-radiopaque lesion's appearance. This significantly contrasts with the finding of Macdonald-Jankowski *et al.* [8] in their systematic review by, in which radiolucent appearance predominated. Siar *et al.* [7] also showed that a large proportion of lesions were radiolucent. Mixed lesions are frequently seen in the desmoplastic subtype of conventional ameloblastoma [18]. The reason for the large percentage of patients in this study having a mixed density is unknown, as is the fact that only two lesions were of the desmoplastic subtype.

A large percentage of lesions found in this study showed well-defined, corticated borders and were easily identifiable from the adjacent, unaffected bone. Malik *et al*. [19] and More *et al*. [12] also reported a high proportion of these lesions showing this feature. The majority of tumours that exhibited unclear margins were associated with larger lesions. These lesions appeared to destroy the cortices and involve the surrounding soft tissue. It may be argued that, due to the expansile nature of this tumour, larger lesions tend to destroy the cortex, which in turn gives rise to an unclear margin.

In this study, just over two-thirds of lesions appeared multilocular on pantomographs. This is comparable to other studies [11,20]. The data in the literature however is conflicting. Some studies indicate a multilocular predominance, whereas others [21,22], indicate that the unilocular appearance is more prevalent. Even though there was no statistically significant association ($p = 0.391$) between lesion's aspect and age, it is evident in our sample that in a younger age category, the majority of lesions appeared as unilocular entities. Tatapudi *et al*. [20] also showed that the unilocular entity occurs at a younger age when compared to the multilocular variety.

According to Worth [5], the "spider-like" pattern is the most common radiological appearance. This is followed by the "soap-bubble" pattern. However, in our study the "soap-bubble" pattern predominated (68.32%). The "spider-like" pattern was present in only a small percentage (10.69%). In addition, the "soap-bubble" pattern presented almost equally in both radiolucent and radiolucent-radiopaque (mixed) lesions.

Ameloblastomas that have caused either only root resorption or root resorption associated with tooth displacement amounted to a substantial proportion (66.38%). In a study by Struthers and Shear [23], it was shown that the incidence of root resorption in association with ameloblastomas was high (81%). Therefore, the inclusion of ameloblastoma as part of a differential diagnosis is essential when root resorption occurs in the presence of a cystic lesion, especially if the posterior region of the mandible is involved.

A study by Fulco *et al*. [24] reported the average size of ameloblastoma as 43 mm. The results of this study showed that the average size of the lesions (86.39 mm) was more than twice the average size reported in the literature. This difference in size could possibly be attributed to late consultation as a result of limited access to advanced healthcare.

Amongst the histopathological subtypes in this review, the CA was found most frequently (48.65%). Within this subtype, the follicular variant was predominant (51.39%). This is in accordance with other studies in the literature [10,24,25]. The plexiform variant was the second most prevalent (16.66%) in this study. In contrast, Saghravanian *et al*. [26] showed that the plexiform pattern was the most commonly occurring variant (41.93%).

Only a small percentage (12.84%) of lesions were diagnosed as UA. However, Tatapudi *et al*. [21], Chawla *et al*. [11] and Krishnapillai [9] showed that UA represented respectively 37%, 34% and 36% of their cohort. According to their results, the UA was the most commonly occurring subtype.

Routine panoramic radiography is part of the diagnostic investigation for pathology screening. However, panoramic radiography cannot rule out other diagnoses whose radiological features can be similar to that of ameloblastomas [27]. These include odontogenic keratocyst, fibromyxoma, fibrosarcoma, haemangioma, aneurysmal bone cyst and giant cell tumour. In addition, other limitations include the inadequate visualisation of bony margins of the tumour, as well as unclear interface between the tumour and normal soft tissue. Furthermore, ameloblastomas have a tendency to perforate the cortex, which is an important feature in order to make a differential diagnosis. This feature cannot always be visualised by conventional radiography [28]. CBCT, CT and MRI are much more efficient in defining differential diagnoses [28]. Another disadvantage of conventional radiography is the inability to assess the internal contents of the lesion. Contrast-enhanced CT and MRI are modalities, which are helpful in this regard [29]. Although advanced imagery is required in most cases, it is not feasible due to the lack of availability and the high cost.

Conclusion

The majority of features of mandibular ameloblastoma in this population were similar to those previous reported in the literature. Major differences included the high predilection for the lesion to occur in black African patients with a higher number of mixed density lesions compared to other studies. The size of lesions in this sample was considerably larger than other reports. Ameloblastoma should always be considered as a differential diagnosis when radiolucent and mixed density lesions are observed in the mandible especially when expansion of the cortex occurs and the presence of root resorption is evident.

Conflict of interest

The authors declare that they have no conflicts of interest in relation to this article.

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