Journal of
Oral Pathology & Medicine **WILEY**

Ameloblastic carcinoma: A systematic review

Liam Robinson[1,2] | Lucas Guimarães Abreu[3] | Felipe Paiva Fonseca[1,4] |
Keith D. Hunter[1,2,5] | Melvin A. Ambele[1] | Willie F. P. van Heerden[1,2]

[1]Department of Oral and Maxillofacial Pathology, School of Dentistry, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

[2]Members of an International Consortium on Odontogenic Tumours

[3]Department of Paediatric Dentistry, School of Dentistry, Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil

[4]Department of Oral Surgery and Pathology, School of Dentistry, Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil

[5]Liverpool Head and Neck Centre, Molecular and Clinical Cancer Medicine Unit, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, UK

Correspondence
Liam Robinson, Pretoria Oral Health Care Centre, Corner of Steve Biko and Dr Savage Road, Pretoria 0084, South Africa.
Email: liam.robinson@up.ac.za

Abstract

Background: Ameloblastic carcinoma (AC) is the most common odontogenic malignancy, constituting approximately 30% of cases in this category. Literature is sparse on malignant odontogenic neoplasms, with a large proportion of current knowledge derived from case reports or small case series.

Methods: A systematic review of case series/case reports of AC was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement guidelines. Demographic and clinical information, including duration of the lesion, location, clinical presentation and radiologic features, were analysed. Additionally, the origin of the lesion (primary/secondary), Ki-67 proliferation index, treatment performed, metastasis, tumour recurrence and prognosis were collected for analysis.

Results: A total of 126 studies, including 285 individual cases of AC, were included in this review. Patients presented with a near-equal distribution of painless and painful swellings. ACs presented at a median age of 45 years, with a male-to-female ratio of 1:2. The mandible was most frequently involved, with rare cases extending to involve more than one region, including crossing the midline. Although most lesions presented with poorly-demarcated borders (52.6%), unilocular lesions with well-demarcated borders (47.4%) comprised a substantial number in the sample. The proliferation index was only reported in 27 cases, with a mean score of 42% and a wide range. The probability of tumour recurrence increased, and the survival probability decreased with prolonged follow-up duration.

Conclusion: This study provides more comprehensive, up-to-date descriptive data on these rare odontogenic malignancies, aiding clinicians and Pathologists with the diagnosis and surgeons in their management of cases.

KEYWORDS
ameloblastic carcinoma, head and neck cancer, odontogenic neoplasms, recurrence rates, survival probability

1 | INTRODUCTION

Definitions and classifications of malignant odontogenic neoplasms have changed over the years, emanating in the current 5th edition of the World Health Organization (WHO) Classification of Head and Neck Tumors. This latest edition included ameloblastic carcinoma (AC), primary intraosseous carcinoma (not otherwise specified), sclerosing odontogenic carcinoma, clear cell odontogenic carcinoma (CCOC), ghost cell odontogenic carcinoma, odontogenic sarcomas, and odontogenic carcinosarcoma within the category of malignant odontogenic tumours. AC is the most common in this group of odontogenic malignancies, constituting approximately 30% of all cases in this category. The latest edition of the WHO classification simply defines AC as a primary odontogenic carcinoma histologically resembling ameloblastoma (AB).[1] ACs are further subdivided into primary cases that arise de novo and secondary cases arising in an untreated or recurrent AB.[1–5]

ACs often present with accompanying signs and symptoms, including paraesthesia in cases involving the mandible, trismus, epistaxis, dysphonia and even pathologic fractures.[4,6–8] Radiographically, they present as ill-defined radiolucent lesions, often with evidence of accompanying cortical perforation and soft tissue infiltration (Figure 1A).[2,8]

Most cases of AC have been treated via extensive local excision with variable safety margins depending on the site of the tumour.[4,6,9] Many authors consider AC radioresistant, limiting the use of this treatment modality to cases unsuitable for surgical intervention or patients with advanced local or metastatic disease.[4,10,11] The role of chemotherapy in treating AC is debatable and has not been indicated as a primary treatment modality.[6]

AC has a relatively high recurrence rate, ranging between 40% and 60%.[12–14] Distant metastases have been reported in approximately 33% of cases, predominantly involving the lungs.[12–15] Studies around the prognosis of ACs have reported a 5-year survival rate of approximately 70%.[4,9,15]

The rarity of AC limits the reported literature to case reports or small case series. Therefore, a recent, up-to-date systematic review summarising the clinicopathologic presentation, treatment and prognosis of ACs is necessary. In this context, this systematic review integrates the current available published data in the literature on AC to provide important information on the clinical and radiologic features, treatment, recurrence frequency, and survival of this malignant odontogenic tumour.

2 | MATERIALS AND METHODS

This systematic review of case series and case reports of AC was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement guidelines.[16]

2.1 | Databases and search strategies

In May 2023, computerised searches were performed in the following electronic databases: Scopus (Elsevier), Web of Science (Clarivate Analytics), PubMed (National Library of Medicine), and Embase (Elsevier). The keyword 'ameloblastic carcinoma' was used in all searches. Open Grey and Google Scholar searches were limited to the first 100 hits.[17] Manual searches of the reference lists of the included articles, attempting to find any article that might have been missed during the computerised searches, were also conducted. The references with titles/abstracts were imported to the software EndNote Web (Clarivate Analytics, London, UK), and duplicates were removed.

2.2 | Eligibility criteria

Articles depicting case series or case reports of AC with adequate clinical, radiologic, and histopathologic data to confirm the diagnosis of AC were eligible for inclusion. The diagnosis of AC was based on the current 5th edition of the WHO classification, whereby AC should show moderate cellular or nuclear atypia, nuclear hyperchromatism, increased mitotic figures, and crowding of the basal cell layer with expansion (Figure 1B). Central tumour necrosis supports the diagnosis of AC, but is not an essential criterion.[1] Additionally, articles needed to be in English for inclusion.
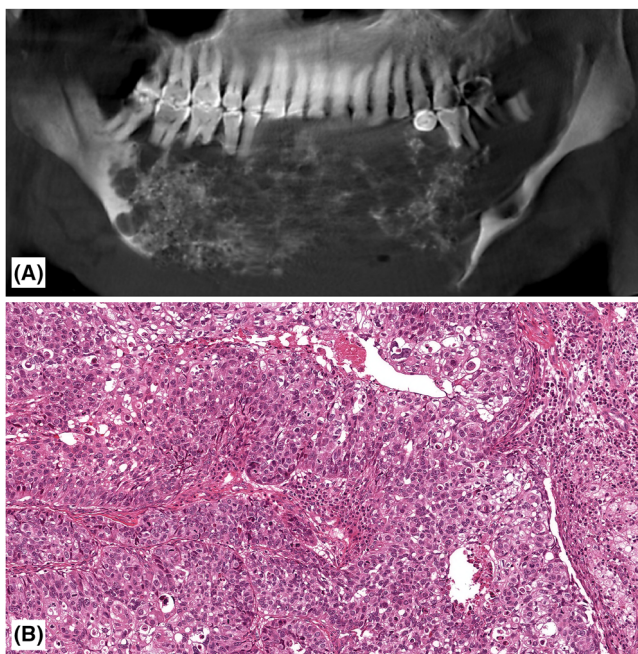

FIGURE 1 (A) Panoramic reconstruction from CBCT volumetric data showing a case of AC affecting the mandible. (B) Histopathologic features of a case of AC. Note the severe cytologic atypia with abundant mitotic figures and focal areas of central necrosis (H&E staining; original magnification: 200×).

Finally, letters to the editor, literature reviews, in vitro studies, and animal studies were excluded.

2.3 | Study selection

The study selection for this review consisted of two phases. In phase 1, the titles/abstracts of the studies found were assessed by two researchers (LR & LGA), who applied the eligibility criteria. If the title/abstract fulfilled the eligibility criteria, the reference was immediately included in the present systematic review. In phase 2, the complete text was retrieved for studies whose titles/abstracts had insufficient information to decide on inclusion/exclusion. After evaluating the complete text of such studies, those that fulfilled the eligibility criteria were also included in the systematic review. Discrepancies of opinion between the two researchers were resolved via consultation with a third researcher (WvH), an experienced Oral and Maxillofacial Pathologist.

2.4 | Data extraction

For each study included, the following data, when available, were extracted on a standard form: authors' name, publication year and country where the case(s) was/were reported. Additionally, the number of case(s) reported, patients' age and sex, duration of the lesion before diagnosis, and the anatomical location (maxilla/mandible) were recorded. For the anatomical location, data was detailed according to the following parameters: site (anterior: lesions in the incisor and canine region; posterior: lesions in the premolar/molar/retromolar/ramus/condyle region; and anterior and posterior: lesions at both sites). The clinical presentation and radiologic features, including borders (well-defined/poorly-defined), density (radiolucent/radiopaque/mixed), locularity (unilocular/multilocular), bone effects (expansion/cortical thinning/cortical destruction), tooth effects (missing/root resorption/tooth displacement/tooth impaction) were also recorded. Finally, the origin of the lesion (primary/secondary), Ki-67 proliferation index (as a percentage), treatment performed, metastasis (yes/no and location), tumour recurrence (yes/no), follow-up period (months), and the individual's status (dead/alive) were noted.

2.5 | Quality assessment

The included studies were critically appraised using the Joanna Briggs Institute – University of Adelaide tool for case reports or case series.[18] The included studies were evaluated according to the following parameters: clear description of the patient's demographic characteristics, clinical presentation, histopathologic analysis with representative description or images required to render a diagnosis of AC, treatment, and post-intervention clinical condition. For each parameter, the included study was rated as 'yes', 'no', 'unclear', or 'not applicable'.

2.6 | Data analysis

Data pooling was performed using MedCalc statistical software (MedCalc Software, Ostend, Flanders, Belgium). The first author conducted a descriptive analysis, aggregating data on the demographic and clinical characteristics of the cases. Kaplan–Meier tests were used to calculate the recurrence probability and the overall and disease-free survival rates combined among the cases.

3 | RESULTS

3.1 | Study selection

The computerised searches retrieved 1425 references, among which 850 were duplicates (Figure 2). Thus, in phase 1, the eligibility criteria were applied to the title/abstract of 575 references. In phase 2, after removing 292 studies whose title/abstract did not meet the eligibility criteria, the final full text of 283 studies was assessed. Of the 283 full text studies, 157 were excluded as they did not meet the eligibility criteria as described above. Finally, a total of 126 studies were included in this systematic review (Supplementary Table 1).

3.2 | Critical appraisal of the included studies

Nearly all cases from included studies (284/285; 99.6%) clearly described the patients' demographic characteristics. Two hundred and
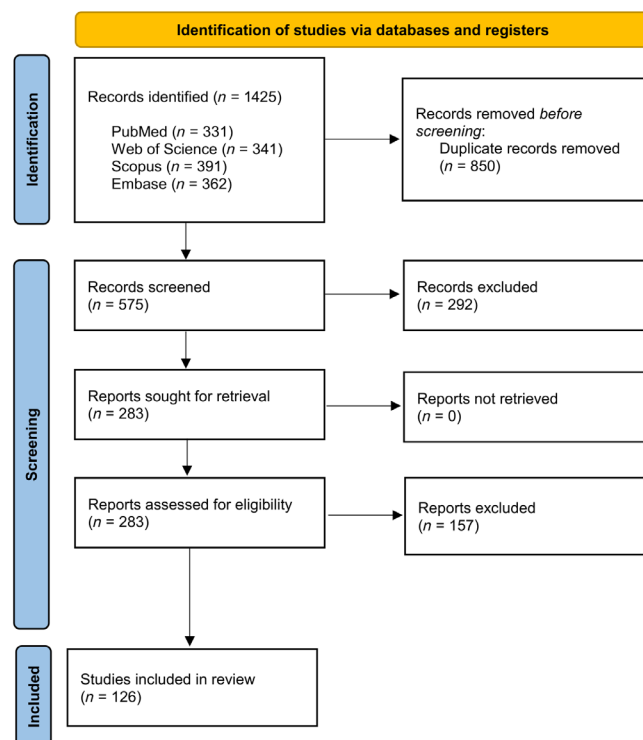

FIGURE 2 Flowchart showing the results of the search process.

sixteen cases (75.8%) reported the clinical presentation. Histopathologic analysis was available for all included cases. Information regarding the treatment and post-intervention clinical condition was reported in 242 (84.9%) and 163 (57.2%) cases, respectively.

3.3 | Demographic and clinicopathologic characteristics

The results of data pooling on the demographic and clinical characteristics are displayed in Table 1. From the final 126 eligible studies, a total of 285 individual cases of AC were included for analysis. Articles from five continents (including 31 countries) were included. Most cases were reported in Asia, followed by the Americas, Africa, Europe, and Oceania.

The mean and median age of affected individuals were 46.1 and 45 years, respectively, with a female predominance. The mean clinical duration of the lesion was 28.3 months and ranged from 0 to 372 months. The mandible was affected in the majority of individuals. The posterior region of the jaws was affected in most cases, with the anterior regions less commonly affected. In 19.3% of cases, the lesion extended to involve both the anterior and posterior regions of the jaws, with 4.6% of cases crossing the midline. The reported clinical signs and symptoms varied amongst the patients, with many reporting more than one symptom. A nonspecific swelling was most frequently reported, followed closely by either a painless or painful lesion. Paraesthesia and ulceration were reported in 8.3% and 6.9% of cases, respectively. Other less common signs and symptoms included tooth mobility, a non-healing extraction socket, headache, and epistaxis. Tumour recurrence was reported in 2.8% of cases, whereas two cases presented as an incidental finding.

Table 2 summarises the radiologic features of included cases of AC. There was a slight predominance of cases presenting with poorly-demarcated borders. Most cases appeared purely radiolucent, with only a minority appearing as mixed radiolucent–radiopaque or with internal calcifications. Unilocular lesions were more often encountered than multilocular lesions. Bony expansion and cortical destruction were commonly seen, whereas cortical thinning was only reported in 12.2% of cases. The most common effects on the surrounding dentition were loss of associated teeth and root resorption. Tooth displacement and tooth impaction were only reported in 14.5% and 11.8%, respectively.

The histopathologic diagnosis, treatment, and metastatic rate are summarised in Table 3. Among the 285 individual cases, 96.1% were diagnosed as conventional AC and 3.9% as the spindle cell variant of AC. Most cases were considered primary ACs, and 24.3% were considered secondary to ameloblastoma. The mean proliferation index was 42%, ranging from 5% to 80%. The majority of cases underwent excision/resection of the tumour alone, with 18.2% of cases treated via resection followed by postoperative radiotherapy. A minority of cases were treated via resection followed by postoperative radiotherapy and chemotherapy, and resection followed by chemotherapy alone. Radiotherapy and chemotherapy as single-modality treatment options were rare. Three cases were deemed inoperable or not amenable to chemo/radiotherapy and were treated palliatively. Of the 215 cases with

available information, 84.2% reported no evidence of metastases, whereas 15.8% had histologically confirmed metastatic deposits.

3.4 | Probability of recurrence

The mean follow-up time for tumour recurrence was 65.74 months (standard error = 6.52). Figure 3 shows the curve for the probability of

TABLE 1 Summarised demographic data and clinical features.

Demographic/clinical feature	n (of cases)	%
Continent[a]		
Asia	134	47.0
Europe	21	7.4
Americas	78	27.4
Africa	46	16.1
Oceania	6	2.1
Age (years)—mean (SD); median (range)[a]	46.1 (19.8)	45.0 (2.0–93.0)
Sex (M:F)[b]	95:189	1:2
Clinical duration of the lesion (months)—mean (SD); median (range)[c]	28.3 (51.0)	6.0 (0.0–372.0)
Site		
Mandible[b]	202	71.1
Maxilla[b]	82	28.9
Anterior[d]	26	11.9
Posterior[d]	140	64.2
Both[d]	42	19.3
Crosses midline[d]	10	4.6
Clinical signs and symptoms[e,f]		
Swelling	107	49.5
Painful	88	40.7
Painless	89	41.2
Ulceration	15	6.9
Paraesthesia	18	8.3
Tooth mobility	5	2.3
Tumour recurrence	6	2.8
Epistaxis	2	0.9
Incidental finding	2	0.9
Headache	2	0.9
Non-healing extraction socket	4	1.9
Bleeding mass, dizziness, vision loss, sinusitis, sinus congestion, rapid growth, vertigo	1 each	0.5

[a]285 cases.
[b]284 cases.
[c]148 cases.
[d]218 cases.
[e]216 cases.
[f]Patients reported more than one symptom.

TABLE 2 Summarised radiologic features.

Radiologic features	n	%
Borders[a]		
Well-demarcated	72	47.4
Poorly-demarcated	80	52.6
Radiodensity[b]		
Radiolucent	153	96.2
Internal calcifications	2	1.3
Mixed (radiolucent–radiopaque)	4	2.5
Locularity[a]		
Unilocular	89	58.6
Multilocular	63	41.4
Bone effects[c,d]		
Bony expansion	109	88.6
Cortical thinning	15	12.2
Cortical destruction	97	78.9
Tooth effects[d,e]		
Loss of teeth	51	67.1
Tooth displacement	11	14.5
Tooth impaction	9	11.8
Root resorption	25	32.9

[a]152 cases.
[b]159 cases.
[c]123 cases.
[d]More than one bone effect/tooth effect recorded.
[e]76 cases.

recurrence. The probability of recurrence at 12 months of follow-up was 22.7%. Within the 120-month follow-up period, the probability of recurrence was 79.1%.

3.5 | Survival probability

Regarding patient survival, data from 163 individuals were pooled. Figure 4 shows the curve for the survival probability. Among the 163 individuals, 41 had died, and 122 were alive. The mean follow-up time was 147.42 months (standard error = 21.58). The survival probability at 12 months of follow-up was 93.0%. Within the 141-month follow-up period, the survival probability was 25.2%.

4 | DISCUSSION

In general, literature on malignant odontogenic neoplasms is sparse, with a large proportion of the current knowledge derived from case reports or small case series.[19] This emphasises the need for systematic reviews to collate published literature on these rare neoplasms, extrapolate findings, and continuously update current knowledge.

AC accounts for less than 2% of all odontogenic tumours,[1,19] and approximately 30% of all malignant odontogenic tumours.[1,2,4] From

TABLE 3 Histopathologic diagnosis, patient treatment and metastatic rate.

Histopathologic diagnosis, treatment and metastatic rate	n	%
Diagnosis[a]		
Ameloblastic carcinoma (conventional type)	274	96.1
Spindle cell variant of ameloblastic carcinoma	11	3.9
Manifestation[b]		
Primary	174	75.7
Secondary	56	24.3
Ki-67 IHC (mean, range)[c]	42%	5–80
Treatment[d]		
Biopsy only	1	0.4
Conservative/enucleation	7	2.9
Excision/resection only	175	72.4
Resection and chemotherapy alone	3	1.2
Resection and radiotherapy alone	44	18.2
Resection, radiotherapy and chemotherapy	4	1.7
Radiotherapy only	3	1.2
Chemotherapy only	2	0.8
Palliative care	3	1.2
Metastasis[e]		
No	181	84.2
Yes	34	15.8

Abbreviation: IHC, immunohistochemistry.
[a]285 cases.
[b]230 cases.
[c]27 cases.
[d]242 cases.
[e]215 cases.
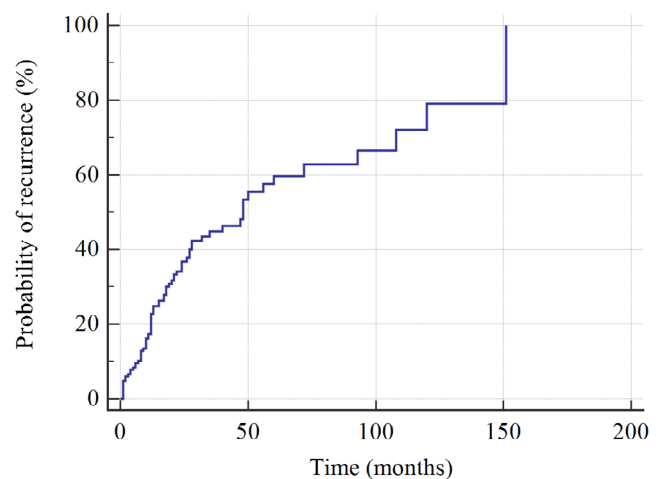
FIGURE 3 Probability curve indicting tumour recurrence.

this systematic review, there were 126 studies consisting of 285 reported cases of AC in the literature. Only 7 publications reported on 10 or more patients.[4,6,11,14,20–22] Asia was the dominant
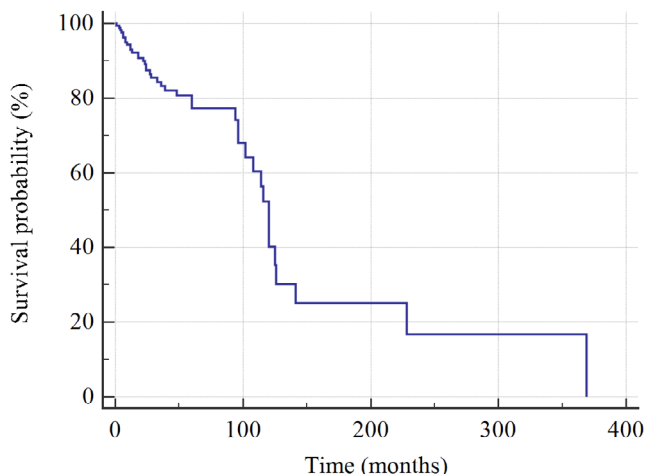
FIGURE 4 Probability curve indicating patient survival.

continent regarding the number of reported cases, comprising 47% of all samples, in keeping with the reported literature.[19,23,24]

Most of the published literature reports similar male-to-female ratios of AC cases of approximately 2:1,[9,12] with an isolated Chinese study reporting a male-to-female ratio of 5:1.[11] In contrast, the current systematic review found an inverse ratio, whereby females predominated with twice as many cases. A previous review of ACs by Giridhar et al.[9] reported a median age of presentation of 49 years, similar to that of the North American study by Hall et al.[23] Other studies, including an Armed Forces Institute of Pathology (AFIP) study by Corio et al. and a sub-Saharan African study, have reported comparatively low mean ages of 30.1 and 37 years, respectively.[6,25] The current systematic review found a median age of 45 years with a wide age range of 2–93 years, with figures falling between previous reports. Interestingly, from this systematic review, 20 cases fell below the age of 18 years, with the youngest case being reported at the age of 2 years.

The mandible was most frequently involved, with a mandible-to-maxilla ratio of approximately 2.5:1. These findings were similar to those reported in other studies.[9,12] This ratio was significantly lower than a Chinese study that reported a mandible-to-maxilla ratio of 11:1,[11] which appears to be an outlier in the literature based on all the selected studies in this review. Regardless of which jaw bone was involved, most cases affected the posterior region, mirroring the previously reported literature.[11,15,24] Interestingly, this systematic review found that 19.3% of cases extended to involve both the anterior and posterior regions of the jaw bones, with 4.6% of cases crossing the midline. These figures have not been previously alluded to in the literature.

In contrast to benign odontogenic tumours, large systematic analyses regarding the clinicoradiologic features of AC are limited.[4] Compared to cases of AB, ACs usually present as painful swellings.[15,19] This systematic review showed that most patients presented with either painless (41.2%) or painful (40.7%) swellings. Patients often present with accompanying signs and symptoms, particularly nerve paralysis in cases involving the mandible.[4] Associated nerve paraesthesia and ulceration in the current review were symptoms secondary to painless/painful swellings at 8.3% and 6.9%, respectively. The current review

highlighted some interesting radiologic findings, in that although 52.6% of cases had poorly-demarcated borders, a substantial percentage of cases (47.4%) still maintained well-demarcated borders. Generally, well-demarcated radiologic borders point to benign processes; therefore, these results suggest a possible caveat in interpreting cases with well-demarcated borders. Additionally, 58.6% of cases presented as unilocular lesions, in contrast to the review study by Akrish et al., who found that only 33% of ACs were unilocular.[12] Interestingly, four cases presented with a mixed radiolucent–radiopaque appearance, likely due to reactive bone formation or the presence of dystrophic calcifications. Bony expansion paired with cortical destruction were common findings, in keeping with a malignant neoplastic process. Furthermore, loss of teeth (67.1%) and root resorption (32.9%) were also frequently reported. Interestingly, tooth displacement and associated tooth impaction were reported in 14.5% and 11.8% of cases, respectively, which are features more commonly described in benign entities.

The histopathologic diagnosis of cases in this review found that 96.1% of cases were diagnosed as so-called conventional AC, with 3.9% of cases being classified as the spindle cell variant of AC. Slater first proposed this term in 1999, distinguishing spindle cell AC from odontogenic carcinosarcoma by lacking the ameloblastic fibrosarcoma-like pattern in the carcinomatous component.[26] A study of three cases of spindle cell AC by McLean-Holden et al. postulated that the spindle cell change likely occurred due to prominent epithelial-mesenchymal transition (EMT) of the neoplastic cells.[27] More cases of this rare variant of AC need to be reported to fully elucidate its biological behaviour, if different from the conventional variant of AC.

In general, literature reports that most cases of ACs arise de novo, with reports of secondary ACs being much rarer.[2,15] A large review study by Akrish et al. of 38 cases of AC reported that most cases arose de novo.[12] In contrast, a South American review study of 31 cases of AC found that more than 75% were classified as the secondary subtype.[28] In this current review, most cases (75.7%) arose de novo, and secondary cases were significantly rarer, representing 24.3% of the current sample.

The current review recorded the Ki-67 proliferation index for 27 cases only, which is low considering its proposed use as an adjunct in diagnosing AC. The mean value was 42%, considerably higher than the means of 21.6%–23.5% previously reported in the literature.[8,28] Unfortunately, there appeared to be a wide range of 5%–80%, indicating limitations of using this marker alone as a diagnostic tool. Casaroto et al. postulated that this wide percentage range may be partly due to the subjective interpretation of the stain.[28]

Most cases reported in this study were treated via surgical resection alone, followed by resection of the tumour with radiotherapy, modalities most frequently reported in the literature.[4,6,9] Radiotherapy or chemotherapy as single modality treatment options were exceedingly rare. These findings are unsurprising as many authors consider AC radioresistant, limiting its use to cases unsuitable for surgical intervention or patients with advanced local or metastatic disease.[4,10,11] Additionally, the role of chemotherapy in treating AC is debatable and has not been indicated as a primary treatment modality, but instead forms part of the palliative regimen.[6] More recently, several novel

targeted treatment modalities have been explored, emanating from a deeper understanding of the molecular pathogenesis of odontogenic lesions. In cases of AB, the high frequency of *BRAF* mutations supports its use as a therapeutic target, particularly in unresectable or recurrent cases.[29] Although ACs have a much lower *BRAF* mutational burden, targeted therapy may still be an indication for cases with proven mutations utilising BRAF inhibitors.[4,6]

ACs with distant metastasis have been reported in approximately 33% of cases, as early as 4 months and as late as 47 months.[12–15] The lungs are the most common site for metastases, with rare cases metastasising to the brain or bones.[15,30–32] In this review, metastatic tumour deposits were significantly rarer, reported in only 15.8% of cases. Unfortunately, the literature was often not descriptive regarding the site of the reported metastatic deposit.

ACs have a relatively high recurrence rate, ranging between 40% and 60%. To this end, local recurrence has been detected between 5 and 151 months, indicating a broad period of tumour recurrence.[12–14] These features concurred with those reported in this review, where the probability of recurrence increased from 22.7% at 12 months follow-up to 79.1% within a 120-month follow-up period.

Isolated studies around the prognosis of ACs have reported a 5-year survival rate of approximately 70%.[4,9,15] A study by Giridhar et al. found a median progression-free survival rate of 57 months and a median overall survival of 122 months for the entire cohort.[9] Of note, in this study, patients younger than 45 years were found to have a better overall survival rate than elderly patients.[9] In this review study, the survival probability at 12 months follow-up was excellent at 93%. Unfortunately, this survival probability decreased to 25.2% after a period of greater than 10 years follow-up. However, the follow-up periods in this study were ambiguous, which may have ultimately skewed the final results.

Although AC represents the most common subtype of odontogenic malignancy, its aetiopathogenesis has still not been fully elucidated. Additionally, cases of AC with frank malignant features rarely pose diagnostic dilemmas; however, difficulty still exists in diagnosing cases with intermediate cytologic features. Conclusive studies centring around ancillary techniques, such as immunohistochemical stains and molecular analyses, are required to clarify the aetiopathogenesis of AC and assist in the workup of diagnostically challenging cases.

5 | CONCLUSION

In summary, this study systematically analysed 285 individual cases of AC, with most cases emanating from the Asian continent. Interestingly, most cases were reported in female patients, in contrast to previously reported literature. This review also reported cases extending to involve more than one region of the jaw bones, including cases that crossed the midline. Another noteworthy finding was the substantial number of cases presenting as unilocular radiolucent lesions with well-demarcated borders, contrasting the usual radiologic presentation of malignant lesions. The proliferation marker Ki-67 was only performed on a minority of cases, unfortunately showing a wide distribution range and limiting its utility as a diagnostic marker. Most cases were treated

via surgical resection alone in support of current treatment regimens. The incidence of metastatic deposits was considerably lower than reported in the literature. Tumour recurrence rates increased, and survival probability decreased as the follow-up period was prolonged.

This study provides important information that could aid clinicians and Pathologists in diagnosing such lesions, and subsequently guide surgeons in managing these rare odontogenic malignancies. Additional studies are needed to expand and solidify the current understanding of AC.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/jop.13517.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

This study was approved by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference no. 228/2023). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008. This article does not contain any studies with human or animal subjects performed by any of the authors.

ORCID

Liam Robinson https://orcid.org/0000-0002-0549-7824
Lucas Guimarães Abreu https://orcid.org/0000-0003-2258-8071
Felipe Paiva Fonseca https://orcid.org/0000-0002-6657-4547
Keith D. Hunter https://orcid.org/0000-0002-7873-0877
Melvin A. Ambele https://orcid.org/0000-0002-6636-2026
Willie F. P. van Heerden https://orcid.org/0000-0003-2494-667X

REFERENCES

1. Odell EW. Chapter 7: Odontogenic and maxillofacial bone tumours. *World Health Organization Classification of Tumours Editorial Board. Head and Neck Tumours*. 5th ed. Lyon (France): International Agency for Research on Cancer; 2022.
2. Richardson MS, Muller S. Malignant odontogenic tumors: an update on selected tumors. *Head Neck Pathol*. 2014;8(4):411-420.
3. Soluk-Tekkesin M, Wright JM. The World Health Organization Classification of Odontogenic Lesions: a summary of the changes of the 2022 (5th) edition. *Turk Patoloji Derg*. 2022;38(2):168-184.
4. Niu Z, Li Y, Chen W, et al. Study on clinical and biological characteristics of ameloblastic carcinoma. *Orphanet J Rare Dis*. 2020;15(1):316.
5. Vered M, Wright JM. Update from the 5th edition of the World Health Organization classification of head and neck tumors: odontogenic and maxillofacial bone tumours. *Head Neck Pathol*. 2022;16(1):63-75.
6. Soyele OO, Adebiyi KE, Adesina OM, et al. Ameloblastic carcinoma: a clinicopathologic analysis of cases seen in a Nigerian teaching hospital and review of literature. *Pan Afr Med J*. 2018;31(208):e1-e15.
7. Jindal C, Palaskar S, Kaur H, Shankari M. Low-grade spindle-cell ameloblastic carcinoma: report of an unusual case with immunohistochemical findings and review of the literature. *Curr Oncol*. 2010;17(5):52-57.
8. Martinez-Martinez M, Mosqueda-Taylor A, Carlos-Bregni R, et al. Comparative histological and immunohistochemical study of ameloblastomas and ameloblastic carcinomas. *Med Oral Patol Oral Cir Bucal*. 2017;22(3):e324-e332.
9. Giridhar P, Mallick S, Upadhyay AD, Rath GK. Pattern of care and impact of prognostic factors in the outcome of ameloblastic carcinoma: a systematic review and individual patient data analysis of 199 cases. *Eur Arch Otorhinolaryngol*. 2017;274(10):3803-3810.
10. Wu JY, Chi LH, Pemg BY, Lin YH. Ameloblastic carcinoma of the maxilla—case report. *J Dent Sci*. 2007;2(3):164-170.
11. Li J, Du H, Li P, Zhang J, Tian W, Tang W. Ameloblastic carcinoma: an analysis of 12 cases with a review of the literature. *Oncol Lett*. 2014;8(2):914-920.
12. Akrish S, Buchner A, Shoshani Y, Vered M, Dayan D. Ameloblastic carcinoma: report of a new case, literature review, and comparison to ameloblastoma. *J Oral Maxillofac Surg*. 2007;65(4):777-783.
13. Lee L, Maxymiw WG, Wood RE. Ameloblastic carcinoma of the maxilla metastatic to the mandible—case-report. *J Craniomaxillofac Surg*. 1990;18(6):247-250.
14. Hall JM, Weathers DR, Unni KK. Ameloblastic carcinoma: an analysis of 14 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(6):799-807.
15. Yoon HJ, Hong SP, Lee JI, Lee SS, Hong SD. Ameloblastic carcinoma: an analysis of 6 cases with review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009;108(6):904-913.
16. Page MJ, McKenzie JE, Bossuyt PM, et al. The Prisma 2020 statement: an updated guideline for reporting systematic reviews. *J Clin Epidemiol*. 2021;134:178-189.
17. Haddaway NR, Collins AM, Coughlin D, Kirk S. The role of Google Scholar in evidence reviews and its applicability to grey literature searching. *PLoS One*. 2015;10(9):e0138237.
18. Gagnier JJ, Kienle G, Altman DG, et al. The care guidelines: consensus-based clinical case reporting guideline development. *J Med Case Reports*. 2013;7:223.
19. Villegas KM, Paparella ML. Malignant odontogenic tumors. A report of a series of 30 cases and review of the literature. *Oral Oncol*. 2022;134:106068.
20. Ndukwe KC, Adebiyi EK, Ugboko VI, et al. Ameloblastic carcinoma: a multicenter Nigerian study. *J Oral Maxillofac Surg*. 2010;68(9):2111-2114.
21. Loyola AM, Cardoso SV, de Faria PR, et al. Ameloblastic carcinoma: a Brazilian collaborative study of 17 cases. *Histopathology*. 2016;69(4):687-701.
22. Deng L, Wang R, Yang M, Li W, Zou L. Ameloblastic carcinoma: clinicopathological analysis of 18 cases and a systematic review. *Head Neck*. 2019;41(12):4191-4198.
23. Jing W, Xuan M, Lin Y, et al. Odontogenic tumours: a retrospective study of 1642 cases in a Chinese population. *Int J Oral Maxillofac Surg*. 2007;36(1):20-25.
24. Nagai N, Takeshita N, Nagatsuka H, et al. Ameloblastic carcinoma—case-report and review. *J Oral Pathol Med*. 1991;20(9):460-463.
25. Corio RL, Goldblatt LI, Edwards PA, Hartman KS. Ameloblastic carcinoma: a clinicopathologic study and assessment of eight cases. *Oral Surg Oral Med Oral Pathol*. 1987;64(5):570-576.
26. Slater LJ. Odontogenic malignancies. *Oral Maxillofac Surg Clin North Am*. 2004;16(3):409-424.
27. McLean-Holden AC, Bishop JA, Kessler HP, et al. Spindle-cell variant of ameloblastic carcinoma: a report of 3 cases and demonstration of epithelial–mesenchymal transition in tumor progression. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2019;128(3):e113-e121.
28. Casaroto AR, Toledo GL, Filho JL, Soares CT, Capelari MM, Lara VS. Ameloblastic carcinoma, primary type: case report, immunohistochemical analysis and literature review. *Anticancer Res*. 2012;32(4):1515-1525.
29. Guimaraes LM, Coura BP, Gomez RS, Gomes CC. The molecular pathology of odontogenic tumors: expanding the spectrum of Mapk pathway driven tumors. *Front Oral Health*. 2021;2:740788.
30. Datta R, Winston JS, Diaz-Reyes G, et al. Ameloblastic carcinoma: report of an aggressive case with multiple bony metastases. *Am J Otolaryngol*. 2003;24(1):64-69.
31. Goldenberg D, Sciubba J, Koch W, Tufano RP. Malignant odontogenic tumors: a 22-year experience. *Laryngoscope*. 2004;114(10):1770-1774.
32. Devenney-Cakir B, Dunfee B, Subramaniam R, et al. Ameloblastic carcinoma of the mandible with metastasis to the skull and lung: advanced imaging appearance including computed tomography, magnetic resonance imaging and positron emission tomography computed tomography. *Dentomaxillofac Radiol*. 2010;39(7):449-453.