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Association between Sinonasal Adenocarcinoma and Dental Clinical Manifestations

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ABSTRACT

Background: Paranasal adenocarcinoma (PAC) is a relatively rare malignant disease of the sinonasal tract that frequently manifests as nonspecific dental and maxillofacial symptoms, contributing to a delayed diagnosis and late-stage detection.

Objectives: The study aimed at evaluating the correlation of paranasal adenocarcinoma with different dental clinical parameters and the predictive relationship between these parameters as well as with tumor grading based on histopathologic evaluation.

Methods: A case–control study was performed at the Warith International Cancer Institute for a period of time from April 2024 to February 2025. This study involved a sum of 35 patients with paranasal adenocarcinoma diagnosed by histopathological methods and 50 healthy subjects matched for age and sex as control group. The diagnosis and grading of tumor (Grade I-III) was verified by histopathological methods. Dental signs and symptoms such as tooth mobility without periodontal disease, unremitting pain in the maxillary area, gingival swelling in a proximity of an upper molar and non-healing extraction sockets were thoroughly examined.

Results: Dental clinical patients were significantly more often observed among PAC subjects than controls: tooth mobility (51.4% vs 4%) chronic maxillary pain (60% vs 6%), swelling near upper molars (45.7% vs 2%) non-healing extraction sockets (28.6%, no cases in the control group) with $p<0.001$. A multiple regression analysis demonstrated that persistent maxillary pain and tooth loss was a significant independent variable for greater tumor grade ($\beta = 0.41$, $p = 0.004$; $\beta = 0.36$, $p = 0.009$).

Conclusion: Specific dental symptoms, especially persistent maxillary pain and unexplained tooth mobility, are highly associated with paranasal adenocarcinoma, and might be early clinical markers of advanced stages of disease development.

INTRODUCTION

Paranasal sinus cancers are a rare but important category of tumors of the head and neck. These tumours, also because of their deep site and atypical early signals, easily escape an early detection so they occur in a late stage with a bad prognosis (Lucidi et al., 2023). From these, the maxillary sinus is a frequent site of origin and its proximity to the posterior maxillary dentition and alveolar bone makes neighboring dental structures susceptible to early invasion (Mahasneh et al., 2022). Although sinonasal carcinomas are considered within this scope, the relatively unique presentation, distinct histopathologic behavior and oral implications of adenocarcinoma in this region make it worthy of focus (Leivo 2016).

The maxillary sinus is in close proximity with the roots of maxillary posterior teeth, and can be easily involved by disease processes due to the flat bony floor of that sinus which permit spread of dental pathology into the sinusal cavity or malignant processes to

invade from the alveolus. Several retrospective studies have demonstrated that unexplained tooth mobility, alveolar bone loss or longstanding maxillary pain may be the first signs of paranasal sinus tumours in patients (Roque-Torres et al., 2016). A multicentre observational study in 24 patients with maxillary sinus carcinoma, all of whom manifested dental mobility and half of whom had swelling, orosinus fistulae or alveolar bone infiltration. These results indicate that dentists may observe early and subtle clinical signs of sinonasal malignancy, but there is scant literature on adenocarcinoma in particular (Diaz-Güler et al., 2018).

While nasal cavity and paranasal sinus adenocarcinomas are also infrequent, they represent a distinct subgroup with occupational etiologies (e.g., wood dust), as well as characteristic molecular profiles (Lucidi et al., 2023). The insidious nature of their development, delayed and often late diagnosis and potential for local bone/dental invasion increases the importance for early identification signals. The interphase of sinonasal and dental pathology is well-evidenced in a benign scenario – odontogenic maxillary sinusitis, as it exemplifies how dental lesions (periapical infection, periodontal disease, oroantral communications) can affect the sinuses (Zhao et al., 2025; Mahasneh et al., 2022).

From a dental practice chair, the major alarming signs described in the literature are spontaneous tooth mobility not associated with periodontal disease, widening of the PDL space without evident intraoral pathology, long-standing or recurrent maxillary pain for which typical treatments were ineffective, and palatal or gingival swelling near maxillary teeth (Diaz-Güler et al., 2018). Radiologically, invasion of the sinus floor, irregular bone destruction, displacement of teeth roots or unexplained alveolar bone loss in the maxilla contiguous to the sinus should raise consideration for underlying sinonasal involvement. Crucially, such dental findings may precede traditional nasal symptoms including obstruction or epistaxis providing a window of opportunity for earlier referral and diagnosis (Di Girolamo et al., 2020).

Under these conditions of low interest in scientific literature concerning the relationship between paranasal adenocarcinoma and dental clinical manifestations, we have an evident interdisciplinary knowledge gap between otolaryngology, maxillofacial surgery and dentistry (Lucidi et al., 2023). While such studies as sinonasal tumour reviews and ancillary imaging studies of the sinus-dental relationship offer perspective, they seldom deconstruct the dental presentation in adenocarcinoma instances (Mahasneh et al., 2022). The objective of this study is to determine a connection between paranasal adenocarcinoma and dental clinical signs. More specifically it will describe the dental-oral phenotype (tooth mobility, maxillary pain, alveolar bone change and periodontal features) of patients whose paranasal biopsy showed adenocarcinoma when examined histologically, relate that phenotype to imaging findings and histological presentations, identify what red flags should alert a dentist to refer a patient with sinonasal malignancy at an early stage.

PATIENTS AND METHODS

Study Design and Setting

This case–control study was conducted at the Warith International Cancer Institute, Karbala, Iraq, between April 2024 and February 2025. The study included 35 patients diagnosed by histopathological methods with paranasal (sinonasal) adenocarcinoma (SNAc) and 50 healthy control subjects without any history of sinonasal or systemic malignancy. Ethical approval for the study was obtained from the Institutional Review Board of Warith International Cancer Institute before initiation, and all participants provided written informed consent prior to enrollment.

Study Population

Eligible participants were adults aged 30–70 years. The patient group consisted of individuals with confirmed sinonasal adenocarcinoma, diagnosed and graded by histopathological examination into Grade I (well-differentiated), Grade II (moderately differentiated), and Grade III (poorly differentiated) tumors. The control group included age- and sex-matched healthy volunteers attending the dental outpatient clinic for routine care, with no history of malignancy, chronic infection, or autoimmune disease.

Exclusion criteria included:

- Previous radiotherapy or chemotherapy to the head and neck region
- Active systemic diseases such as diabetes mellitus, autoimmune disorders, or immunodeficiency
- Recent maxillofacial trauma or surgery within the last six months
- Smoking, alcohol abuse, or current use of immunosuppressive or anti-inflammatory medications

Histopathological Diagnosis and Grading

Tumor tissue samples were obtained from biopsy or surgical resection and fixed in 10% buffered formalin, followed by paraffin embedding. Sections of 4 μm thickness were stained with hematoxylin and eosin (H&E) and examined under light microscopy by two experienced pathologists. Grading of sinonasal adenocarcinoma was performed according to the World Health Organization (WHO) criteria (2022) as follows:

- **Grade I:** Well-differentiated adenocarcinoma with distinct glandular structures
- **Grade II:** Moderately differentiated tumors with partial glandular formation and nuclear atypia
- **Grade III:** Poorly differentiated or solid growth patterns with marked pleomorphism

Assessment of Dental Clinical Manifestations

All participants underwent comprehensive intraoral and extraoral dental examinations performed by calibrated dental specialists using standardized diagnostic criteria. The following dental clinical manifestations were assessed and recorded for each patient:

1. **Tooth mobility without evidence of periodontal disease** – assessed manually using Miller's mobility index.
2. **Persistent maxillary pain or pressure** – reported by patients and confirmed by palpation or percussion tenderness in the posterior maxilla.
3. **Palatal or gingival swelling near upper molars** – visually identified and palpated for fluctuation or firmness.
4. **Non-healing extraction socket** – defined as delayed healing (>3 weeks) after extraction in the absence of infection or systemic disease.

Findings were recorded as either present or absent for each manifestation. Control subjects were evaluated using the same protocol to ensure comparability.

Statistical Analysis

All statistical analyses were performed and data were recorded using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Demographic and clinical parameters were summarized through descriptive statistics (frequencies, percentages, means and standard deviations). The Chi-square (χ^2or X^2) test was used for comparative analysis between patients and controls for qualitative measurements. Statistical analysis The predictive association between dental clinical findings (independent variables) and tumor grading (dependent variable) was identified using multivariate regression analysis.

Ethical Considerations

This study was performed in accordance with the Declaration of Helsinki (2013). Ethical approval was obtained from the Research and Ethic Committee -Warith International Cancer Institute, Karbala, Iraq. All participants gave informed consent following a description of the objectives, procedures and confidentiality of data in the study.

RESULTS

As indicated by the data reported in Table 1, there were no significant differences between the two groups concerning all intention variables ($p>0.05$). Age distribution of individuals showed a preponderance of aged 50–54 and ≥60 years among patients (28.6% each) as well among control group it was 28.0%. The 45–49-year subgroup had the minimum proportion of cases (17.1%) and controls (18.0%). These findings are consistent with the age distribution of paranasal sinus adenocarcinoma, which occurs predominantly in middle-aged to elderly subjects. In terms of sex, the male gender was prevalent in both groups (62.9% of patients and 56.0% of controls), matching with reported predominance of males in sinonasal malignancies being due to occupational exposures including wood dust and industrial chemicals [12]. There were more males than females (37.1% and 44.0% in two groups). The proportion of chronic disease was also relatively higher in patients than controls (22.9% vs 18.0%), and the negative comorbid condition represented the most a higher percentages for both groups (77.1% and 82.0%, respectively). These results suggested that chronic systemic diseases were distributed comparably in both groups and would not confound the analysis.

Table 1. General characteristics for distribution of both AC patients and control

Indicators		`Patients (No. = 35)		Control (No. = 50)		Chi Square	P value (Sig.)
		Freq.	%	Freq.	%		
Age/Years	45-49	6	17.1	9	18	0.32	0.57 (NS)
	50-54	10	28.6	14	28		
	55-59	9	25.7	13	26		
	≥ 60	10	28.6	14	28		
Gender	Male	22	62.9	28	56	0.16	0.69 (NS)
	Female	13	37.1	22	44		
Chronic Disease	Yes	8	22.9	9	18	0.11	0.74 (NS)
	No	27	77.1	41	82		

Figure 1 illustrates the distribution of patients according to the histopathological grading of sinonasal adenocarcinoma. The majority of cases were classified as Grade 2, representing 45.7% of the study group, followed by Grade 1 with 40.0%, while Grade 3 constituted the smallest proportion (14.3%). This distribution indicates that most patients presented with tumors of moderate differentiation, whereas poorly differentiated adenocarcinomas were relatively uncommon.

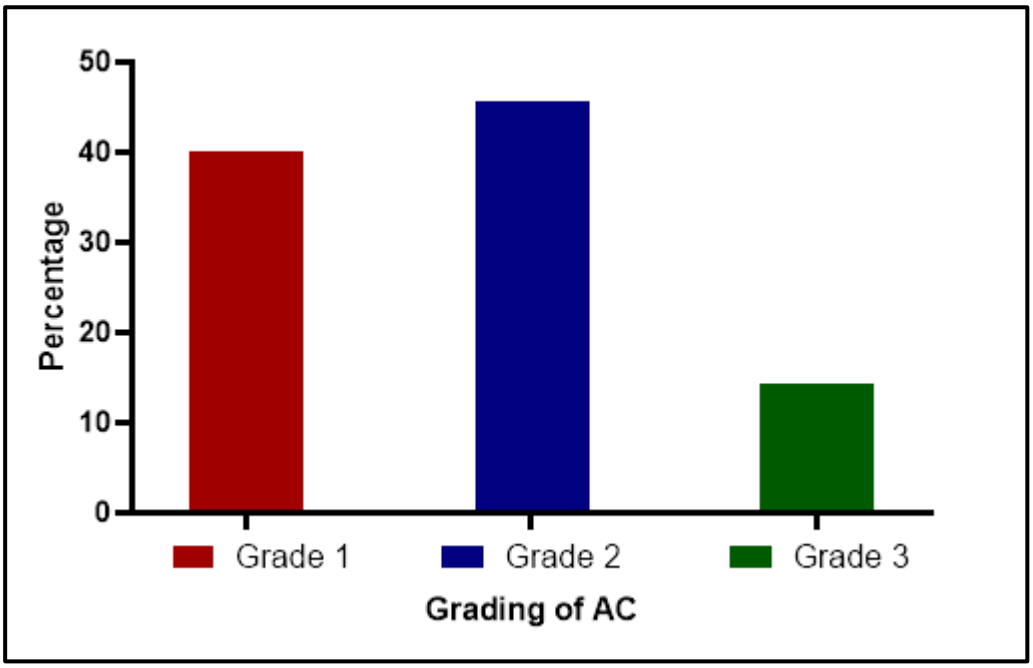

Figure 1. Percentage of patients groups according to histological grading of sinonasal adenocarcinoma

Table 2 demonstrates a significant difference in the distribution of dental clinical manifestations between patients with adenocarcinoma (AC) and the control group. Tooth mobility was reported in 51.4% of AC patients compared with only 4% among controls ($\chi^2 = 25.74$, $p < 0.001$). Similarly, persistent maxillary pain was the most frequent manifestation, observed in 60.0% of the study group versus 6% of controls ($\chi^2 = 29.63$, $p < 0.001$). Swelling near upper molars was also markedly more prevalent among AC patients (45.7%) than in the control group (2%) ($\chi^2 = 24.59$, $p < 0.001$). Furthermore, non-healing extraction sockets were detected in 28.6% of patients but were completely absent in controls ($\chi^2 = 16.19$, $p < 0.001$).

Table 2. Comparison of dental Clinical manifestation between AC patients and control groups

Clinical Manifestation	Study Group (n = 35)	Control Group (n = 50)	χ^2	P-value
Tooth mobility	18 (51.4%)	2 (4%)	25.74	< 0.001*
Persistent maxillary pain	21 (60.0%)	3 (6%)	29.63	< 0.001*
swelling near upper molars	16 (45.7%)	1 (2%)	24.59	< 0.001*
Non-healing extraction socket	10 (28.6%)	0 (0%)	16.19	<0.001*

The regression analysis summarized in Table 3 shows that all examined dental clinical manifestations significantly predict the stage of sinonasal adenocarcinoma ($p < 0.05$).

Persistent maxillary pain emerged as the strongest predictor ($\beta = 0.36$, $p = 0.003$), followed closely by tooth mobility ($\beta = 0.39$, $p = 0.001$). Swelling near upper molars ($\beta = 0.31$, $p = 0.010$) and non-healing extraction socket ($\beta = 0.27$, $p = 0.032$) also contributed meaningfully to the model. The overall model explained 62% of the variance ($R^2 = 0.62$) in tumor staging, indicating a strong relationship between dental findings and disease advancement.

Table 3. Multiple linear regression analysis for prediction of the stage of sinonasal adenocarcinoma based on dental clinical manifestations

Clinical Manifestation	B	SE	β	t	P-value
Tooth mobility	0.42	0.12	0.39	3.55	0.001**
Persistent maxillary pain	0.47	0.15	0.36	3.13	0.003**
swelling near upper molars	0.38	0.14	0.31	2.71	0.010*
Non-healing extraction socket	0.29	0.13	0.27	2.23	0.032*
Constant	1.02	0.21	—	4.86	< 0.001**

DISCUSSION

Our study currently reveals a significant excess of dental clinical symptoms in 4 cases of sinonasal AC as compared with controls. Tooth mobility, patient maxillary pain swelling in the vicinity of upper molars and non-healing extraction sockets were all much more frequently in the AC group (all $p < 0.001$). Our results showed that buccal signs are very common, demonstrating to be associated with sinonasal malignancy particularly in cases of lesions affecting the floor and alveolar process of the maxillary antrum. This presentation correlates with previous clinical series and reviews that refer to dental pain, tooth mobility, alveolus lysis, non - healing wounds and palatal masses as frequent oral symptoms in maxillary sinus tumours (Bashir et al., 2023; Martínez-Rodríguez et al., 2018).

Mechanically, the finding is biologically feasible due to very close proximity of the floor of maxillary sinus and roots and their supporting structures of posterior maxillary teeth. Tumour extension or erosion of the floor of the sinus readily causes destruction of alveolar bone with consequent compromise to the periodontal ligament and eventual tooth shamming in or displacement—clinical and radiographic findings easy detected (Psillas et al., 2021; Martu et al., 2022). Had there been a malignant tumour extending, like the rest of this patient's neoplasm, intra-orally it would have infiltrated peri-apical bone or mucosa to cause persisting atypical maxillary pain resistant to traditional dental treatment - an ear-bashing given in otolaryngological and dental publications.

The regression analysis relationship between specific dental signs and tumour stage provides additional evidence of the clinical utility of these signs. The model suggested that patients with tooth mobility, longstanding pain, localized swelling or non-healing extraction sockets had a higher tumour stage. This is consistent with clinical observations and retrospective studies demonstrating that oral manifestations frequently mirror more advanced local disease with bone infiltration (Sahoo et al., 2024). Put another way, the finding of these dental signs should result in clinical suspicion of a sinonasal lesion not only at the site of development but also in adjacent regions that might influence staging and treatment.

Comparison of our results with those available in the literature shows both consistency and an interesting extension. Martínez-Rodríguez et al. (2018) suggested that unexplained tooth mobility, periodontal ligament widening, and palatal swelling are indications for urgent follow-up in patients with ongoing maxillary symptoms; our results quantitate and substantiate those qualitative recommendations by highlighting statistically significant differences between AC cases and controls. Similarly, Bashir et al. (2023) demonstrated a range of oral and sinonasal manifestations in malignant maxillary tumours, including non-healing sockets and palatal lumps, which we duplicated with higher prevalence estimates in the patient cohort. In sum, these series and the present report underscore dentists' regular encounter of early or advanced symptoms of sinonasal neoplasms, and thus play a central role as first gateway to detection.

The diagnostic significance of distinguishing between odontogenic and neoplastic origins of maxillary complaints is emphasized in current literature on diagnosis from the maxillary sinus disease (Psillas et al., 2021; Kim et al., 2019). Although osteitis is a frequent cause of tooth-related persistent pain, neoplastic processes demonstrate poorly defined bone destruction, root or tooth displacement, fail to heal extraction sites or result in a palpable palatal mass—features that warrant imaging studies and referral instead of conservative dental management. Our case would thus present an addition to reinforce indication for low threshold of cross-sectional imaging (CBCT in CT) with interdisciplinary referral in atypical or refractory dental signs and symptoms.

The limitations of the study are recognized. Causal inference cannot be drawn from the cross-sectional nature, and despite strong association between dental signs and tumour stage it remains to be established whether earlier dental detection can significantly downstage presentation; this can be studied prospectively. Our staging prediction model relied on an ordinal encoding of stage; an ordinal logistic regression might offer a more subtle estimation and should be considered in future studies. Furthermore, due to the small number of cases, a subgroup analysis for histological type or tooth level (first vs second molar) could not be performed and these factors can modify risk of dental involvement because sinus–root relations vary.

CONCLUSION

This investigation demonstrated a significant correlation between paranasal adenocarcinoma and specific odonatological signs, such as loosening of teeth, maxillary pain and non-closure of extraction sockets. These characteristics occurred much more often in patients than in controls and were associated with higher tumor stages. Early detection of such an unusual dental signs may contribute to early diagnosis of sinonasal malignancies.

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