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PEDRO HENRIQUE SILVA DE GRÁCIA

NEOPLASIAS DE GLÂNDULAS SALIVARES MENORES: ESTUDO OBSERVACIONAL RETROSPECTIVO DO TRIÂNGULO MINEIRO

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia – Mestrado da Universidade de Uberaba, como requisito para obtenção do título de Mestre em Odontologia, área de Biopatologia.

Orientador: Profº. Dr. João Paulo Silva Servato

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Dissertação apresentada como parte dos requisitos para obtenção do título de Mestre em Odontologia do Programa de Pós-Graduação em Odontologia - Mestrado da Universidade de Uberaba.

Área de concentração: Biopatologia

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Entre o que sou e o que posso ser, no rigor do método e no mistério da vida, caminhando e aprendendo,
permaneço.

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RESUMO

As neoplasias de glândulas salivares menores constituem um grupo raro e heterogêneo, com ampla diversidade histopatológica e comportamento biológico variável. Embora pouco frequentes na cavidade oral, apresentam relevância clínica devido à dificuldade diagnóstica e à maior proporção de malignidade em comparação às glândulas maiores. Este estudo teve como objetivo descrever e analisar retrospectivamente o perfil clinicopatológico das neoplasias intraorais de glândulas salivares menores diagnosticadas em dois serviços de Patologia Oral do Triângulo Mineiro, Brasil. Trata-se de um estudo observacional retrospectivo baseado na análise de prontuários e laudos histopatológicos da Universidade Federal de Uberlândia (UFU; 1978–2024) e da Universidade de Uberaba (UNIUBE; 1999–2024). Foram incluídos casos de neoplasias de glândulas salivares menores, sendo excluídos casos com dados inconsistentes ou incompletos, duplicados e neoplasias de glândulas salivares maiores. Foram revisados 25.168 laudos, dos quais 344 (1,37%) corresponderam a neoplasias de glândulas salivares. Após as exclusões, a amostra final foi composta por 229 casos. As variáveis analisadas incluíram dados sociodemográficos e clinicopatológicos, com análise estatística pelo teste exato de Fisher ($p < 0,05$). Do total, 125/229 casos (54,6%) foram neoplasias benignas e 104/229 (45,4%) malignas. O Adenoma Pleomórfico foi o subtipo mais frequente (40,2%), seguido pelo Carcinoma Mucoepidermoide (14,8%) e pelo Adenocarcinoma Polimorfo (9,6%). Houve predominância do sexo feminino (65,5%), média de idade de 49,3 anos e maior acometimento do palato (47,2%). A maioria das lesões apresentou crescimento nodular (84,3%) e caráter assintomático (78,2%). Observou-se associação significativa entre malignidade e sexo masculino, localização extrapalatina, menor tempo de evolução, presença de sintomas, ulceração, coloração não normocrômica, realização de biópsia incisional e maior frequência de margens comprometidas ($p < 0,05$). Os achados permitiram caracterizar o perfil clinicopatológico das neoplasias de glândulas salivares menores na população estudada, evidenciando importantes associações relacionadas à malignidade.

Palavras-chave: Neoplasias; Neoplasias das Glândulas Salivares; Epidemiologi

ABSTRACT

Minor salivary gland neoplasms constitute a rare and heterogeneous group of lesions with wide histopathological diversity and variable biological behavior. Although uncommon in the oral cavity, they are clinically relevant due to diagnostic challenges and the higher proportion of malignancy compared with major salivary glands. This study aimed to retrospectively describe and analyze the clinicopathological profile of intraoral minor salivary gland neoplasms diagnosed in two Oral Pathology services from the Triângulo Mineiro region, Brazil. This retrospective observational study was based on the analysis of medical records and histopathological reports from the Federal University of Uberlândia (UFU; 1978–2024) and the University of Uberaba (UNIUBE; 1999–2024). Cases of minor salivary gland neoplasms were included, while cases with inconsistent or incomplete data, duplicate cases, and major salivary gland neoplasms were excluded. A total of 25,168 reports were reviewed, of which 344 (1.37%) corresponded to salivary gland neoplasms. After exclusions, the final sample comprised 229 cases. Sociodemographic and clinicopathological variables were analyzed using Fisher's exact test ($p < 0.05$). Of the total, 125/229 cases (54.6%) were benign neoplasms and 104/229 (45.4%) were malignant. Pleomorphic adenoma was the most frequent subtype (40.2%), followed by mucoepidermoid carcinoma (14.8%) and polymorphous adenocarcinoma (9.6%). There was a predominance of females (65.5%), a mean age of 49.3 years, and greater involvement of the palate (47.2%). Most lesions presented nodular growth (84.3%) and were asymptomatic (78.2%). Significant associations were observed between malignancy and male sex, extrapalatal location, shorter duration, presence of symptoms, ulceration, non-normochromic coloration, incisional biopsy, and higher frequency of compromised surgical margins ($p < 0.05$). The findings allowed the characterization of the clinicopathological profile of minor salivary gland neoplasms in the studied population, highlighting important associations related to malignancy.

Keywords: Neoplasms; Salivary Gland Neoplasms; Epidemiology

SUMÁRIO

1 INTRODUÇÃO

A região maxilofacial é composta por diversas estruturas anatômicas que, em conjunto, formam um sistema integrado. Entre essas estruturas, destacam-se as glândulas salivares, responsáveis por funções essenciais, como secreção salivar, lubrificação, proteção dos tecidos orais e participação em processos imunológicos. Essas glândulas subdividem-se em dois grupos: as seis glândulas salivares maiores, dispostas em pares (parótida, submandibular e sublingual), e centenas de glândulas salivares menores, distribuídas em diferentes áreas da face e da cavidade oral (COLLAZO-FERNANDEZ *et al.,* 2017).

As glândulas salivares são suscetíveis a diferentes alterações patológicas, incluindo processos inflamatórios, alterações degenerativas e neoplasias. Embora não sejam extremamente comuns, as neoplasias de glândulas salivares não podem ser consideradas raras, representando aproximadamente 3 a 6% de todos os tumores de cabeça e pescoço, com incidência mundial estimada entre 0,4 e 13,5 casos por 100.000 habitantes (OLIVEIRA *et al.,* 2009; VASCONCELOS *et al.,* 2016; SILVA *et al.,* 2018; BRUZINGA *et al.,* 2021; SANTANA *et al.,* 2021).

Recentemente, a Organização Mundial da Saúde (OMS) atualizou a classificação dos tumores de glândulas salivares, reconhecendo 31 neoplasias epiteliais primárias distintas, evidenciando a complexidade morfológica e biológica dessas lesões. Essa diversidade histológica reforça a heterogeneidade dos tumores salivares e destaca os desafios envolvidos em seu diagnóstico e classificação (FIELD *et al.,* 2024).

Quanto à distribuição por localização, observa-se que 64 a 80% das neoplasias acometem a glândula parótida, 7 a 11% as glândulas submandibulares, cerca de 1% a glândula sublingual e 9 a 23% as glândulas salivares menores. Em relação ao comportamento biológico, as neoplasias de glândulas salivares menores apresentam predomínio de tumores benignos, que correspondem a mais de 50% dos casos, enquanto as neoplasias malignas representam uma parcela menor, porém clinicamente relevante (VARGAS *et al.,* 2002; ITO *et al.,* 2005; OLIVEIRA *et al.,* 2009; VASCONCELOS *et al.,* 2016; VIVEIROS *et al.,* 2019; BRUZINGA *et al.,* 2021).

Embora relativamente incomuns na população geral, as neoplasias malignas de glândulas salivares menores apresentam prevalência estimada entre 0,16 e 2,6 casos por 100.000 habitantes, evidenciando sua baixa ocorrência, mas reforçando sua importância

diagnóstica e clínica (VARGAS *et al.,* 2002; ITO *et al.,* 2005; OLIVEIRA *et al.,* 2009; VASCONCELOS *et al.,* 2016; VIVEIROS *et al.,* 2019; BRUZINGA *et al.,* 2021).

No Brasil, país de dimensões continentais e marcado por ampla diversidade geográfica, cultural e populacional, observa-se variação significativa na frequência das neoplasias de glândulas salivares. Estudos epidemiológicos indicam que esses tumores correspondem a aproximadamente 0,25% a 2,6% de todas as lesões diagnosticadas em serviços de patologia oral, sendo que as neoplasias malignas representam entre 28,9% e 57,7% dos tumores de glândulas salivares menores, dependendo da região analisada (LOIOLA *et al.,* 2009; DA SILVA *et al.,* 2018; CUNHA *et al.,* 2020).

No âmbito específico das neoplasias de glândulas salivares menores, a ocorrência média situa-se entre a quarta e a sétima décadas de vida, com predileção pelo sexo feminino e maior acometimento no palato e no lábio superior (SILVA *et al.,* 2018). Apesar desses padrões clínico-epidemiológicos relativamente bem estabelecidos, a etiologia dessas lesões permanece pouco esclarecida, reforçando a importância da investigação de seus mecanismos de desenvolvimento e fatores associados (LARSEN *et al.,* 2010).

Diversos estudos na literatura apresentam dados sobre a frequência dos tumores de glândulas salivares. Entretanto, grande parte dessas pesquisas analisa conjuntamente tumores de glândulas salivares maiores e menores, sendo que a maioria das amostras é composta predominantemente por tumores originados nas glândulas maiores (VARGAS *et al.,* 2002; SANTOS *et al.,* 2003; BARBOSA *et al.,* 2005; ITO *et al.,* 2005; LIMA *et al.,* 2005; LOIOLA *et al.,* 2009; AGRIPINO *et al.,* 2010; MORAIS *et al.,* 2011; FONSECA *et al.,* 2012; MELO e*t al.,* 2012; LIMA *et al.,* 2015; VASCONCELOS *et al.,* 2016; BARIN *et al.,* 2017; SILVA *et al.,* 2018; REINHEIMER *et al.,* 2019; CUNHA *et al.,* 2020; RODRIGUES *et al.,* 2022; BRAZÃO *et al.,* 2023). Dessa forma, estudos que avaliam exclusivamente neoplasias de glândulas salivares menores ainda são relativamente escassos e frequentemente apresentam amostras limitadas, o que dificulta uma compreensão mais precisa da epidemiologia dessas lesões LOYOLA *et al.,* 1995; NÓBREGA *et al.,* 2010; ABRAHÃO *et al.,* 2016; SARMENTO *et al.,* 2016; VIVEIROS *et al.,* 2019; BRUZINGA *et al.,* 2021).

Do ponto de vista clínico, a diferenciação inicial entre neoplasias benignas e malignas pode ser desafiadora, uma vez que ambas geralmente se apresentam como massas de crescimento lento, indolores e recobertas por mucosa de aspecto normal, podendo eventualmente apresentar ulceração. A duração da lesão é variável e, muitas vezes, o diagnóstico definitivo depende da avaliação histopatológica (OMITOLA *et al.,* 2018).

Entre as neoplasias mais frequentemente observadas em glândulas salivares menores destacam-se, no grupo das benignas, o Adenoma Pleomórfico (AP) e o Adenoma Canalicular (AC), enquanto entre as malignas sobressaem o Carcinoma Mucoepidermoide (CME), o Carcinoma Adenoide Cístico (CAC) e o Adenocarcinoma Polimorfo (AcP) (VIVEIROS *et al.,* 2019).

O Adenoma Pleomórfico (AP) é a neoplasia benigna mais prevalente das glândulas salivares, podendo acometer tanto crianças quanto adultos, sem predileção sexual definida (LENNON *et al.,* 2015). Também denominado tumor benigno misto, acomete principalmente o palato, o lábio superior e a mucosa jugal. Clinicamente, caracteriza-se como uma massa firme, indolor e de crescimento lento, podendo ocorrer de forma solitária, sincrônica ou metacrônica (EL-NAGGAR *et al.,* 2017). O tratamento consiste na excisão cirúrgica com margens livres, devido ao risco de transformação maligna, estimado entre 5% e 6,2% dos casos. Apesar do prognóstico geralmente favorável, a taxa de recidiva pode alcançar até 43% (VIVEIROS *et al.,* 2019).

O Adenoma Canalicular (AC) também é uma neoplasia benigna caracterizada histologicamente por células epiteliais ductais monomórficas organizadas em cordões sobre estroma frouxo, vascularizado e com escassa celularidade (REGEZI *et al.,* 2012). Clinicamente, apresenta-se como aumento de volume indolor, de crescimento lento, firme ou flutuante, com mucosa adjacente de coloração normal ou azulada (NEVILLE *et al.,* 2016). É mais prevalente em indivíduos acima dos 50 anos, com predileção pelo sexo masculino, acometendo principalmente o lábio superior e a mucosa jugal. O tratamento é cirúrgico, com excelente prognóstico e baixa taxa de recidiva (EL-NAGGAR *et al.,* 2017).

O Carcinoma Mucoepidermoide (CME) é a neoplasia maligna mais frequente das glândulas salivares, sendo o palato o sítio de maior ocorrência quando relacionado às glândulas salivares menores (CUNHA *et al.,* 2020). Afeta pacientes de diferentes faixas etárias, principalmente entre a segunda e a sétima décadas de vida, com maior prevalência no sexo feminino (LENNON *et al.,* 2015). Histologicamente, é composto por células mucosas, intermediárias e epidermoides, organizadas em padrões císticos e sólidos (ADELSTEIN *et al.,* 2012). Clinicamente, pode apresentar-se como lesão assintomática, de desenvolvimento lento e coloração azulada, semelhante a uma mucocele. O tratamento consiste em excisão cirúrgica ampla, associada à radioterapia em casos avançados, devido ao potencial metastático. O prognóstico depende do grau histológico e do tipo de glândula acometida, sendo geralmente mais favorável nos casos envolvendo glândulas salivares menores (GATTA *et al.,* 2020).

O Carcinoma Adenoide Cístico (CAC) é uma neoplasia maligna caracterizada clinicamente por aumento de volume de crescimento lento, frequentemente acompanhado de dor ou parestesia (CAWSON; ODELL, 2013). Histologicamente, apresenta células epiteliais e mioepiteliais organizadas em padrões sólido, tubular ou cribiforme (NEVILLE *et al.,* 2016). Predomina no sexo feminino, com média etária de aproximadamente 57 anos, embora também possa ocorrer em crianças. Apesar de ser mais comum em glândulas salivares maiores, cerca de um terço dos casos ocorre em glândulas menores, com predileção pelo palato. O tratamento envolve excisão cirúrgica radical, frequentemente associada à radioterapia. A taxa de metástases varia entre 35% e 50%, com taxas de sobrevida estimadas em 60 a 80% em cinco anos, 50 a 70% em dez anos, 25 a 40% em quinze anos e cerca de 25% em vinte anos (WANG *et al.,* 2015).

O Adenocarcinoma Polimorfo (AcP) é uma neoplasia maligna caracterizada por crescimento infiltrativo e padrão celular relativamente uniforme, porém com grande variabilidade morfológica. Localiza-se preferencialmente no palato, mucosa jugal, região retromolar, lábio superior e base de língua, acometendo predominantemente mulheres, com média etária de aproximadamente 59 anos (ABRAHÃO *et al.,* 2016). Clinicamente, apresenta-se como massa indolor de desenvolvimento lento. O tratamento consiste em excisão cirúrgica ampla, com acompanhamento prolongado devido ao risco de recidiva. Apesar disso, apresenta prognóstico geralmente favorável (NEVILLE *et al.,* 2016).

A prevalência e a distribuição das neoplasias de glândulas salivares podem variar significativamente de acordo com fatores como localização geográfica, características populacionais, tipo de serviço de saúde analisado e natureza da instituição responsável pelo diagnóstico, como serviços de patologia oral, centros hospitalares ou unidades especializadas em cirurgia de cabeça e pescoço. Dessa forma, compreender o perfil epidemiológico dessas neoplasias em diferentes regiões torna-se fundamental para ampliar o conhecimento sobre seu comportamento clínico e patológico.

Diante do exposto, o objetivo deste estudo é descrever e analisar os casos diagnosticados retrospectivamente como neoplasias intraorais de glândulas salivares menores, provenientes do Serviço de Estomatologia/Patologia Oral da Universidade Federal de Uberlândia (UFU), no período de 1978 a 2024, e da Universidade de Uberaba (UNIUBE), entre 1999 e 2024.

2 HIPÓTESE / JUSTIFICATIVAS

HIPÓTESE: Segundo Appolinário (2011), estudos descritivos de levantamento podem prescindir da formulação de hipóteses, uma vez que possuem como objetivo principal descrever características, distribuição e comportamento de determinados fenômenos em uma população. De forma semelhante, as recomendações da iniciativa Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) para estudos observacionais não estabelecem a obrigatoriedade de hipóteses formais em pesquisas descritivas retrospectivas, especialmente naquelas com enfoque epidemiológico e clinicopatológico. Dessa forma, considerando o delineamento metodológico adotado, o presente estudo não foi conduzido com hipótese previamente estabelecida, priorizando a descrição e análise do perfil clinicopatológico das neoplasias de glândulas salivares menores na população estudada.

JUSTIFICATIVAS: Estudos epidemiológicos possuem grande importância para a saúde pública e para o desenvolvimento científico, pois permitem compreender o comportamento das doenças em diferentes populações e subsidiar estratégias de prevenção, diagnóstico e tratamento (LIMA *et al.,* 2010). No caso das neoplasias de glândulas salivares, os dados epidemiológicos ainda apresentam ampla variação entre diferentes regiões, possivelmente relacionada a fatores geográficos, populacionais e ao perfil dos serviços responsáveis pelo diagnóstico dessas lesões. Além disso, muitos estudos da literatura analisam conjuntamente tumores de glândulas salivares maiores e menores, sendo relativamente escassas as pesquisas que investigam exclusivamente as neoplasias de glândulas salivares menores, especialmente aquelas conduzidas a partir de delineamentos multicêntricos e com longos períodos históricos de avaliação.

Dessa forma, estudos que avaliem o perfil clinicopatológico dessas lesões em diferentes regiões tornam-se relevantes. Nesse contexto, o presente estudo analisa retrospectivamente casos diagnosticados em dois serviços de referência em Patologia Oral da região do Triângulo Mineiro, abrangendo várias décadas de registros histopatológicos. O caráter multicêntrico e a ampla série histórica analisada possibilitam maior representatividade amostral e contribuem para uma compreensão mais abrangente do perfil epidemiológico e clinicopatológico das neoplasias de glândulas salivares menores na população estudada.

3 OBJETIVOS

3.1 Objetivo Geral:

Descrever e analisar os casos diagnosticados retrospectivamente como neoplasias intraorais de glândula salivar menor, procedentes do Serviço de Estomatologia/Patologia Oral da Universidade Federal de Uberlândia – UFU (1978-2024) e da Universidade de Uberaba – UNIUBE (1999-2024).

3.2 Objetivos Específicos:

Obter dos prontuários informações clínicas e patológicas relevantes, a fim de caracterizar o presente estudo;

Associar os achados clínico-patológicos com o subtipo histológico da neoplasia, buscando identificar possíveis padrões significantes de apresentação;

Analisar comparativamente os achados clinicopatológicos deste estudo à luz de estudos epidemiológicos brasileiros sobre neoplasias de glândulas salivares menores, buscando identificar convergências, divergências e possíveis particularidades regionais no perfil dessas lesões.

4 MATERIAIS E MÉTODOS

População a ser estudada/ Local de realização da pesquisa: Trata-se de um estudo observacional retrospectivo conduzido de acordo com as diretrizes do Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (von ELM *et al.,* 2008). Após aprovação no Comitê de Ética em Pesquisa (CEP), da Universidade de Uberaba, tendo como CAAE: 83277824.2.0000.5145 (Anexo A), os dados foram coletados dos registros clínicos de todos os pacientes com Neoplasia de Glândula Salivar Menor, diagnosticados e tratados pelos serviços: 1- Laboratório de Patologia Oral da Universidade Federal de Uberlândia – UFU (1978-2024) e 2- Laboratório de Patologia Oral da Universidade de Uberaba – UNIUBE (1999-2024) (CID10: C00.9; C02; C03; C04; C05; C06; C06.0; C06.1; C06.2; C06.9; C14). O critério para diagnóstico das lesões citadas acima, seguiu o proposto pela Organização Mundial da Saúde (FIELD *et al.,* 2024).

Garantias éticas aos participantes da pesquisa: Todos os pesquisadores envolvidos tomaram medidas que garantam a liberdade de participação, a integridade do participante da pesquisa e a preservação dos dados que possam identificá-lo, garantindo, especialmente, a privacidade, sigilo e confidencialidade.

Método utilizado: Os dados foram coletados independentemente por dois pesquisadores, com posterior conferência e validação por um supervisor. As informações sociodemográficas e clinicopatológicas dos pacientes participantes foram obtidas por meio da consulta aos prontuários médicos e odontológicos, utilizando-se um instrumento de coleta de dados padronizado (questionário semiestruturado). As variáveis analisadas incluíram idade (em anos), sexo biológico (masculino ou feminino), cor/raça, categorizada de acordo com a classificação adotada pelo Instituto Brasileiro de Geografia e Estatística (IBGE, 2022) e posteriormente agrupada em duas categorias (brancos e não brancos) para fins de análise estatística**,** sintomatologia (presença de tumoração e/ou dor), tipo histológico da lesão, tempo de evolução (em meses), natureza da lesão (primária ou recidiva/persistência), localização anatômica, tamanho da lesão (em centímetros), descrição clínica, tipo de biópsia (incisional ou excisional) e estado das margens cirúrgicas (livres ou comprometidas). Os dados experimentais foram descritos utilizando, quando pertinente, média ± desvio padrão, mediana e percentual. A análise estatística foi realizada utilizando-se o software GraphPad Prism 6.0 (GraphPad Software, San Diego, CA, USA). Para avaliar a associação entre os fatores clinicopatológicos e a natureza das lesões, foi aplicado o teste exato de Fisher, conforme apropriado, considerando-

se o tamanho amostral e a distribuição das frequências esperadas. Adotou-se nível de significância de 5%, sendo considerados estatisticamente significativos os valores de $p < 0,05$.

Critérios de inclusão e exclusão dos participantes da pesquisa: (A) Critérios Inclusão: (a) Todos os pacientes diagnosticados retrospectivamente com Neoplasias de Glândulas Salivares Menores. (CID10: C00.9; C02; C03; C04; C05; C06; C06.0; C06.1; C06.2; C06.9; C14). (B) Critérios Exclusão: (a) Casos demostrando achados clínicos e histopatológicos inconsistentes, ausentes ou com prontuários mal preenchidos; (b) casos duplicados; (c) casos que se configuram como Neoplasias de Glândulas Salivares Maiores.

Revisão da literatura: Para fins de comparação dos achados epidemiológicos obtidos neste estudo, foi realizada uma revisão da literatura. A busca bibliográfica foi conduzida nas bases de dados PubMed/MEDLINE, Scopus e SciELO, incluindo artigos publicados nos idiomas inglês, português e espanhol. Foram utilizados os seguintes descritores e suas combinações: *"minor salivary gland tumors", "minor salivary gland neoplasms", "salivary gland tumors", "salivary gland neoplasms"* e *"epidemiology"*. A busca foi realizada de agosto de 2025 a novembro de 2025, sem restrição inicial de data de publicação. A seleção dos estudos foi realizada por meio da leitura de títulos e resumos, seguida da análise completa dos artigos potencialmente elegíveis para inclusão na discussão comparativa dos resultados. Foram priorizados estudos com amostras representativas e séries de casos publicadas em diferentes populações. Os estudos selecionados tiveram seus principais dados epidemiológicos e clinicopatológicos sistematizados em tabela comparativa, possibilitando a análise das variáveis investigadas, bem como a identificação de semelhanças, divergências e possíveis particularidades entre os achados da literatura e os resultados obtidos no presente estudo.

Riscos e benefícios envolvidos na execução da pesquisa: (A) RISCOS: Toda coleta de dados envolvendo seres humanos acarreta algum tipo de risco, seja ele físico, psíquico, moral, intelectual, social, cultural ou espiritual. Contudo, devido ao seu delineamento retrospectivo, o único possível risco deste projeto seria perda da confidencialidade dos dados, dessa forma, conforme descrito no "Termo de compromisso para utilização de dados de arquivo (prontuários)", os autores se comprometeram a seguir regras explícitas a fim de preservar a privacidade dos dados coletados, de assegurar que as informações foram utilizadas única e exclusivamente para a execução do projeto e de garantir que as informações somente serão divulgadas de forma anônima, não sendo usadas iniciais ou quaisquer outras indicações que possam identificar o sujeito da pesquisa. (B) BENEFÍCIOS: Não existem benefícios diretos para a população estudada, contudo os dados aqui levantados serão importantes para a Sociedade e para a Literatura, pois estes delimitaram quais sujeitos tem maiores risco de

desenvolver neoplasias de glândulas salivares menores, bem como conhecer quais os tratamentos e prognósticos mais comumente utilizados/encontrados neste tipo de paciente. Ademais, ao se conhecer os tratamentos utilizados poderemos evidenciar quais destes são mais efetivos, possibilitando ensaios clínicos efetivos subsequentes (Benefícios indiretos). Critérios de encerramento ou suspensão de pesquisa: não se aplica.

5 ARTICLE

ARTICLE IN ACCORDANCE WITH MEDICINA ORAL PATOLOGÍA ORAL Y CIRUGIA BUCAL - EISSN: 1698-6946 - ANEXO B

5.1 TITLE PAGE

JOURNAL SECTIONS: Oral Medicine and Pathology
ARTICLE TYPE: Research articles
TITLE: Minor Salivary Gland Neoplasms: a retrospective observational study of two pathology services in the triângulo mineiro region
SHORT TITLE: Minor Salivary Gland Neoplasms: A Retrospective Study in Triângulo Mineiro
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5.2 ABSTRACT

Minor salivary gland neoplasms (MSGNs) are uncommon lesions characterized by marked histopathological diversity and variable clinical behavior. This study aimed to analyze the clinicopathological characteristics of MSGNs diagnosed in two Oral Pathology services in Minas Gerais, Brazil. A retrospective review of 25,168 histopathological reports identified 229 cases of MSGNs. Benign tumors accounted for 54.6% of cases and malignant tumors for 45.4%. Pleomorphic adenoma was the most frequent subtype (40.2%), followed by mucoepidermoid carcinoma (14.8%) and polymorphous adenocarcinoma (9.6%). Females were more frequently affected (65.5%), and the palate was the most common anatomical site (47.2%). Statistical analysis demonstrated significant associations between malignancy and male sex, non-palatal location, shorter lesion duration, presence of symptoms, ulceration, and incisional biopsy. Additionally, a literature review was performed for comparative purposes, based on a bibliographic search in PubMed/MEDLINE, Scopus, and SciELO databases, including studies published in English, Portuguese, and Spanish. The search used descriptors related to minor and major salivary gland neoplasms and epidemiology, and studies were selected through title and abstract screening followed by full-text analysis, prioritizing representative case series from different populations. These findings reinforce known epidemiological patterns and highlight clinical features that may assist in the diagnostic suspicion of malignant tumors.

Keywords: Neoplasms; Salivary Gland Neoplasms; Epidemiology

5.3 INTRODUCTION

Salivary glands are essential structures of the stomatognathic system, playing important roles in saliva secretion, lubrication and protection of oral tissues, as well as participating in immunological mechanisms within the oral cavity. These glands are classified into major salivary glands, parotid, submandibular, and sublingual, and numerous minor salivary glands widely distributed throughout the oral mucosa [1]. They are susceptible to a variety of pathological alterations, including inflammatory processes, degenerative changes, and neoplasms. Although not extremely common, salivary gland neoplasms cannot be considered rare, accounting for approximately 3% to 6% of all head and neck tumors, with a worldwide incidence estimated between 0.4 and 13.5 cases per 100,000 inhabitants [2,3,4,5,6].

The complexity of these lesions is highlighted by the recent update of the salivary gland tumor classification by the World Health Organization (WHO), which recognizes 31 distinct primary epithelial neoplasms, reflecting their remarkable morphological and biological diversity [7]. Minor salivary gland neoplasms, in particular, constitute a heterogeneous group of lesions characterized by wide cellular, morphological, and functional diversity [8]. This histological variability may complicate clinical and pathological categorization, representing a significant diagnostic challenge, while their etiology remains poorly understood [2]. Regarding anatomical distribution, most salivary gland neoplasms arise in the parotid gland, whereas minor salivary glands account for approximately 9% to 23% of cases [9].

In Brazil, a country of continental dimensions and marked geographic, cultural, and population diversity, significant variation in the frequency of salivary gland neoplasms has been observed. Epidemiological studies indicate that these tumors correspond to approximately 0.25% to 2.6% of all lesions diagnosed in oral pathology services, with malignant neoplasms representing between 28.9% and 57.7% of tumors affecting minor salivary glands, depending on the region analyzed [10,5,11]. In general, these neoplasms occur more frequently between the fourth and seventh decades of life, with a predilection for females and a higher incidence in the palate and upper lip [5].

From a clinical perspective, the initial differentiation between benign and malignant lesions can be challenging, as both commonly present as slow-growing, painless masses covered by mucosa with normal appearance, with definitive diagnosis often depending on histopathological evaluation [2].

Although numerous studies have reported the frequency of salivary gland tumors in different Brazilian regions, most investigations analyze neoplasms of major and minor salivary

glands together, with samples predominantly composed of tumors arising from major glands [12,13,14,15,11,16,17,18,19,10,20,21,3,22,23,24,25,6]. Consequently, studies focusing exclusively on minor salivary gland neoplasms remain relatively scarce and frequently involve limited sample sizes, which hinders a more precise understanding of the epidemiological profile of these lesions [26,2,27,28,29,9].

Therefore, the aim of this study was to describe and retrospectively analyze cases diagnosed as intraoral minor salivary gland neoplasms from the Oral Pathology/Stomatology Service of the Federal University of Uberlândia (UFU) between 1978 and 2024, and from the University of Uberaba (UNIUBE) between 1999 and 2024.

5.4 MATERIALS AND METHODS

This retrospective observational study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [30] guidelines and was approved by the Research Ethics Committee of the University of Uberaba (UNIUBE), Brazil (CAAE: 83277824.2.0000.5145). All procedures were conducted in accordance with ethical standards for research involving human subjects.

Clinical records and Anatomic Pathology Requisition Forms of patients diagnosed with minor salivary gland neoplasms were retrospectively retrieved from two Oral Pathology services located in Minas Gerais, Brazil: (1) the Oral Pathology Laboratory of the Federal University of Uberlândia (UFU), covering the period from 1978 to 2024, and (2) the Oral Pathology Laboratory of the University of Uberaba (UNIUBE), covering the period from 1999 to 2024. Histopathological diagnoses were established according to the criteria defined in the World Health Organization Classification of Head and Neck Tumours (FIELD et al., 2024).

The inclusion criteria comprised all patients retrospectively diagnosed with minor salivary gland neoplasms (ICD-10 codes: C00.9; C02; C03; C04; C05; C06; C06.0; C06.1; C06.2; C06.9; C14). Cases were excluded when presenting: (1) incomplete, inconsistent, or absent clinical or histopathological data; (2) duplicated records; or (3) neoplasms originating from major salivary glands.

Data collection was independently performed by two researchers and subsequently verified by a supervisor. Sociodemographic and clinicopathological data were obtained from medical and dental records using a standardized data collection form. The variables analyzed included age, sex, race/ethnicity, categorized according to the classification adopted by the Brazilian Institute of Geography and Statistics (IBGE, 2022) [31] and subsequently grouped into two categories (White and non-White) for statistical analysis, symptomatology, histological diagnosis, lesion duration, lesion location, lesion size, clinical description, type of biopsy, surgical margins, and lesion nature (primary or recurrence/persistence).

Descriptive statistics were used to summarize the data, including mean ± standard deviation, median, absolute frequencies, and percentages. Statistical analyses were performed using GraphPad Prism 6.0 software (GraphPad Software, San Diego, CA, USA). Associations between clinicopathological variables were assessed using Fisher's exact test. A significance level of 5% was adopted, and p values < 0.05 were considered statistically significant.

For comparative purposes, a literature review was also conducted using the PubMed/MEDLINE, Scopus, and SciELO databases. Studies published in English, Portuguese,

and Spanish addressing epidemiological and clinicopathological aspects of minor salivary gland neoplasms were selected. The main findings of the included studies were systematically organized in a comparative table to identify similarities, divergences, and epidemiological patterns in relation to the present study.

5.5 RESULTS

Clinicopathological data

A total of 25,168 histopathological reports from two oral pathology services were reviewed, encompassing various types of oral and related lesions. Among these, 383 reports corresponded to salivary gland neoplasms, including cases involving both major and minor salivary glands, as well as duplicate or inadequately documented records.

After excluding 39 reports classified as duplicates (n = 22) or incomplete data (n = 17), 344 valid salivary gland neoplasm cases remained. Subsequently, 115 cases involving major salivary glands were excluded, resulting in a final sample of 229 cases of minor salivary gland neoplasms (MSGNs), which comprised the total sample (N) of the present study.

Considering the overall dataset of 25,168 histopathological reports, MSGNs accounted for 229/25,168 cases (0.91%) of all diagnosed lesions. When analyzed within the subset of 344 valid salivary gland neoplasms, minor salivary gland tumors represented 66.6% of cases (229/344).

Benign neoplasms comprised most of the sample (125/229 cases; 54.6%), whereas malignant neoplasms accounted for 104/229 cases (45.4%) (Table 1). Fourteen histopathological subtypes were identified, including six benign and eight malignant entities. The three most prevalent subtypes were Pleomorphic Adenoma (PA; 92/229 cases; 40.2%), followed by Mucoepidermoid Carcinoma (MEC; 34/229 cases; 14.8%) and Polymorphous Adenocarcinoma (PAC; 22/229 cases; 9.6%). Sixteen cases (7.0%) lacked definitive histological subtype classification but were confirmed as malignant salivary gland neoplasms. A detailed distribution of histological subtypes is presented in Table 1.

Regarding sex distribution, 150/229 cases (65.5%) occurred in females and 79/229 cases (34.5%) in males, yielding a female-to-male ratio of 1.9:1. Benign neoplasms predominantly affected females (91/125; 72.8%), whereas malignant neoplasms demonstrated a more balanced distribution between females (59/104; 56.7%) and males (45/104; 43.3%) (Table 1).

The mean age at diagnosis was 49.3 years (±18.7), ranging from 11 to 87 years. Pleomorphic Adenoma and Mucoepidermoid Carcinoma were most frequently diagnosed during the fifth decade of life, whereas Polymorphous Adenocarcinoma predominated in the seventh decade (Table 1).

Regarding self-reported skin color, 103/229 cases (45.0%) occurred in White individuals and 95/229 (41.5%) in non-White individuals; this information was unavailable in

31 cases (13.5%). Considering only cases with available data, the White-to-non-White ratio was 1.08:1 (103/95) (Table 1).

The palate was the most affected anatomical site (108/229 cases; 47.2%), followed by the lip (35/229; 15.3%), buccal mucosa (33/229; 14.4%), alveolar ridge (17/229; 7.4%), and retromolar region (17/229; 7.4%). A detailed distribution of anatomical sites is presented in Table 2.

Among the three most prevalent histological subtypes, Pleomorphic Adenoma showed marked predilection for the palate (59/92; 64.1%), followed by the lip (12/92; 13.0%) and buccal mucosa (10/92; 10.9%). Mucoepidermoid Carcinoma demonstrated broader distribution, most frequently involving the palate (13/34; 38.2%), retromolar region (9/34; 26.5%), and buccal mucosa (6/34; 17.6%). Adenoid Cystic Carcinoma occurred predominantly in the palate (8/21; 38.1%), followed by buccal mucosa (4/21; 19.0%) and alveolar ridge (3/21; 14.3%) (Table 2).

Regarding symptomatology, 179/229 cases (78.2%) were asymptomatic, whereas 50/229 (21.8%) presented with symptoms. Adenoid Cystic Carcinoma was the subtype most frequently associated with pain or discomfort (13/21; 61.9%), followed by Polymorphous Adenocarcinoma (10/22; 45.5%) and Mucoepidermoid Carcinoma (8/34; 23.5%). Among benign neoplasms, Pleomorphic Adenoma was the most frequent subtype among symptomatic cases (7/92; 7.6%). A detailed distribution of symptomatology, time until diagnosis, lesion size, and clinical manifestation according to histological subtype is shown in Table 3.

The duration of lesions ranged from 0.2 to 480 months, with a mean of 34.1 months (±60.3), and lesion size ranged from 0.2 to 10 cm, with a mean of 2.5 cm (±2.0). Most tumors were classified as primary lesions (211/229 cases; 92.1%), whereas 18/229 cases (7.9%) corresponded to recurrences (Table 3).

Clinically, most lesions presented as nodules (193/229 cases; 84.3%), while 24/229 cases (10.5%) were ulcerated. The predominant color was normochromic (105/229 cases; 45.9%), followed by erythematous lesions (61/229 cases; 26.6%). Sessile base was observed in 67/229 cases (29.3%) and pedunculated base in 9/229 cases (3.9%). The detailed clinical description of the lesions is presented in Table 4.

In the comparative analysis between benign and malignant neoplasms, a complete comparison of clinicopathological variables is presented in Table 5. A statistically significant association was observed between sex and malignancy, with a higher proportion of malignant tumors among males (Fisher's exact test: $p = 0.0123$).

Anatomical location was also significantly associated with tumor nature (Fisher's exact test: $p = 0.0036$), with benign tumors more frequently located in the palate, whereas malignant neoplasms occurred more often in other oral cavity sites. Malignant tumors showed a tendency toward shorter duration of evolution compared to benign lesions (Fisher's exact test: $p = 0.0102$). The presence of symptomatology demonstrated a strong association with malignancy, being significantly more frequent in malignant tumors (Fisher's exact test: $p < 0.0001$). Ulceration was significantly associated with malignant neoplasms (Fisher's exact test: $p = 0.0004$), while nodular presentation was predominantly associated with benign tumors (Fisher's exact test: $p = 0.0004$). Lesion color also differed significantly between benign and malignant groups (Fisher's exact test: $p = 0.0126$) (Table 5).

Regarding biopsy type, incisional biopsies were more frequently performed in malignant tumors (Fisher's exact test: $p < 0.0001$). Among cases submitted to excisional biopsy, compromised surgical margins were significantly more frequent in malignant lesions (Fisher's exact test: $p = 0.0211$). Conversely, variables such as age (Fisher's exact test: $p = 0.083$), skin color (Fisher's exact test: $p = 0.475$), lesion size (Fisher's exact test: $p = 0.582$), lesion base (Fisher's exact test: $p = 0.1587$), clinical margins (Fisher's exact test: $p = 0.0526$), and lesion manifestation (Fisher's exact test: $p = 0.8064$) did not show statistically significant associations with tumor nature (Table 5).

Literature review

The Brazilian literature review identified 25 studies addressing minor salivary gland neoplasms, although only a limited number evaluated exclusively MSGNs across all variables (Table 6). Most studies analyzed salivary gland neoplasms collectively, including both major and minor glands [5,6,12-25], whereas only a few investigations focused exclusively on minor salivary gland tumors [2,9,26-29].

A predominance of studies from the Northeast and Southeast regions was observed. The Northeast accounted for 12/25 studies [3,10-13,18-21,23,28,29], followed by the Southeast with 6/25 studies [2,9,24-27], in addition to the present study. The South region contributed five studies [6,14,15,17,22]. No studies exclusively addressing MSGNs were identified from the North or Center-West regions, indicating an important geographic gap in the Brazilian literature. Some studies included samples from more than one region, such as investigations involving the Southeast and South [16] or both the Northeast and Southeast regions [5].

The absolute number of MSGN cases varied considerably among the reviewed studies, ranging from 6 cases [25] to 1,114 cases [5], with an approximate mean of 150 cases per study. Among studies focusing exclusively on MSGNs, only a few reported large case series, including studies with 687 cases [9] and 480 cases [2]. In this context, the present series comprising 229 cases represents one of the largest Brazilian samples focused exclusively on MSGNs.

The proportion of MSGNs among salivary gland neoplasms also varied substantially across studies, especially among those including both major and minor salivary glands. In mixed samples, the relative frequency of MSGNs generally ranged from approximately 9% to 50% [3,5,6,10-25], whereas studies specifically dedicated to minor salivary gland tumors reported proportions approaching 100% [27,26,9,2]. In the present study, MSGNs represented 66.6% of valid salivary gland neoplasms.

The number of histopathological subtypes reported in Brazilian studies ranged from 3 to 20. Studies with broader diagnostic stratification described 20 [9], 19 [5], and 17 [17] subtypes, while others reported between 13 and 15 entities [2,10,11,22,26]. Conversely, some investigations reported lower histopathological diversity, with only 3 to 6 subtypes identified [13-15,19,23]. The present study identified 14 subtypes, including six benign and eight malignant entities, indicating a broad histopathological spectrum comparable to studies with more detailed diagnostic stratification.

Pleomorphic Adenoma was the most frequent subtype in most Brazilian studies [2,3,5,6,9-12,14-23,26-28], followed mainly by Mucoepidermoid Carcinoma and Adenoid Cystic Carcinoma. In the present study, the three most frequent subtypes were Pleomorphic Adenoma, Mucoepidermoid Carcinoma, and Polymorphous Adenocarcinoma.

Most Brazilian studies reported a predominance of female patients and greater involvement of middle-aged adults [2,3,9,21,26-29]. Similarly, the present study demonstrated female predominance and a mean age of 49.3 years. The palate was consistently described as the most affected anatomical site [2,3,5,6,9,11,14-17,19,22,23,26-29], followed by the lip and buccal mucosa in several studies, a pattern also observed in the present sample.

Clinical presentation was generally characterized by asymptomatic, slow-growing nodular lesions covered by mucosa with normal appearance [5,9,27,29]. Few Brazilian studies performed formal statistical comparisons between benign and malignant MSGNs [2,5,11]. Among those that did, symptomatology was frequently associated with malignant tumors [2,5]. In the present study, malignancy was significantly associated with male sex, extrapalatine

location, shorter lesion duration, presence of symptoms, ulceration, non-normochromic coloration, incisional biopsy, and compromised surgical margins.

5.6 DISCUSSION

Minor salivary gland neoplasms (MSGNs) represent a relatively rare and heterogeneous group of lesions characterized by broad histopathological diversity and variable biological behavior. In the present study, MSGNs accounted for 229/25,168 cases (0.9%) of all diagnosed lesions and 229/344 cases (66.6%) of the salivary gland neoplasms included in the analysis. Although relatively uncommon among oral lesions overall, MSGNs represent a substantial proportion of salivary gland tumors. The multicentric design and the extensive historical period analyzed contribute to the epidemiological robustness of the present series, although the retrospective nature of the study inevitably limited the completeness of some clinical information.

The predominance of benign tumors observed in the present series is consistent with most Brazilian studies evaluating MSGNs [27,28,16,26,6,11,2]. However, the proportion of malignant tumors remained considerable (45.4%), reinforcing the well-established concept that minor salivary gland tumors present proportionally higher malignant potential compared with major salivary gland neoplasms. Variability in the benign-to-malignant ratio across studies likely reflects differences in referral center profiles, inclusion criteria, and methodological heterogeneity, especially among investigations that analyzed tumors from major and minor glands collectively [13,17,21,20,29,5].

The histopathological spectrum observed in the present study reinforces the marked morphological heterogeneity of MSGNs. The identification of 14 subtypes places the present study within the range reported by investigations with broader diagnostic refinement [2,10,11,22,26]. The variability observed among Brazilian studies, ranging from 3 to 20 subtypes [9,5,17], likely reflects not only biological diversity but also methodological differences, such as grouping of entities, exclusion of rare tumors, and differences in histopathological classification criteria.

Pleomorphic Adenoma was the most frequent subtype, followed by Mucoepidermoid Carcinoma and Polymorphous Adenocarcinoma. This distribution largely agrees with the Brazilian literature, in which Pleomorphic Adenoma consistently represents the predominant MSGN [2,3,5,6,9-12,14-23,26-28]. Nevertheless, some studies identified Mucoepidermoid Carcinoma [21,25,29] or Adenoid Cystic Carcinoma [13] as the most prevalent subtype, particularly in series with proportionally higher frequencies of malignant tumors. These differences likely reflect regional epidemiological variation and distinct diagnostic profiles among institutions.

The predominance of female patients and the mean age around the fifth decade of life are also consistent with previous Brazilian studies [2,3,9,21,26-29]. Although the biological mechanisms underlying this demographic distribution remain unclear, the consistency of these findings across different populations suggests a relatively stable epidemiological pattern. In contrast, skin color did not demonstrate a statistically significant association with tumor nature. Interpretation of this variable remains limited due to incomplete reporting and methodological heterogeneity in the literature [5,15,18,23].

The palate was the most affected anatomical site, followed by the lip and buccal mucosa, corroborating previous Brazilian reports [2,3,5,6,9,11,14-17,19,22,23,26-29]. This distribution is anatomically expected due to the high concentration of minor salivary glands in the palatal region. Clinically, this finding reinforces the importance of including MSGNs in the differential diagnosis of persistent palatal swellings.

Most lesions in the present study were asymptomatic, nodular, non-ulcerated, and covered by mucosa with normal coloration, which corresponds to the classical clinical presentation of MSGNs [5,9,27,29]. In addition, the prolonged lesion duration observed in many cases reinforces the indolent clinical behavior frequently associated with these tumors. Such characteristics may delay clinical suspicion and diagnosis, emphasizing the importance of biopsy in persistent intraoral nodules, even when clinically innocuous.

Most tumors corresponded to primary lesions, while recurrence rates remained relatively low. However, interpretation of recurrence data should be performed cautiously due to the retrospective design and lack of standardized follow-up. Recurrence in salivary gland tumors is influenced by multiple factors, including histological subtype, infiltrative growth pattern, adequacy of surgical margins, and duration of follow-up [2,25].

The comparative analysis between benign and malignant tumors identified significant associations between malignancy and male sex, extrapalatine location, shorter lesion duration, symptomatology, ulceration, non-normochromic coloration, incisional biopsy, and compromised surgical margins. Few Brazilian studies have performed inferential analyses evaluating associations between clinicopathological variables and tumor nature [2,5,11]. Among these, symptomatology has also been associated with malignant tumors [2,5], supporting the interpretation that symptomatic lesions may reflect more aggressive biological behavior.

The association between incisional biopsy and malignancy probably reflects the clinical management adopted for lesions with suspicious features, since tumors clinically suggestive of malignancy are more likely to undergo diagnostic incisional procedures prior to definitive

treatment. Likewise, the higher frequency of compromised surgical margins among malignant tumors may be explained by their infiltrative growth pattern and greater surgical complexity.

Conversely, variables such as age, skin color, lesion size, lesion base, clinical margins, and lesion manifestation did not demonstrate significant associations with tumor nature. These findings reinforce the substantial clinical overlap between benign and malignant MSGNs and demonstrate that isolated clinical characteristics are insufficient to reliably predict biological behavior. Therefore, histopathological examination remains indispensable for definitive diagnosis.

Overall, the present study contributes to the understanding of MSGNs by providing one of the largest multicentric Brazilian series exclusively focused on minor salivary gland neoplasms, with extensive historical coverage and systematic comparison with national epidemiological data. The findings corroborate established epidemiological patterns, such as the predominance of Pleomorphic Adenoma, female predilection, and palatal involvement, while also identifying clinicopathological variables associated with malignancy. These results may contribute to earlier diagnostic suspicion and improved clinical management of MSGNs.

5.7 CONCLUSION

In conclusion, minor salivary gland neoplasms (MSGNs) constitute a heterogeneous group of lesions with distinct clinicopathological features. In the present study, pleomorphic adenoma was the most frequent subtype, and a predominance in females and in the palate was observed, corroborating well-established epidemiological patterns.

Importantly, the comparative analysis between benign and malignant tumors demonstrated that malignancy is significantly associated with male sex, extrapalatinal location, shorter lesion duration, presence of symptoms, ulceration, non-normochromic color, and a higher frequency of incisional biopsies and compromised surgical margins. These findings highlight clinically relevant parameters that may assist in the early suspicion of malignant behavior.

Given the large sample size and the analytical approach adopted, this study contributes to a more refined understanding of MSGNs in the Brazilian population. Clinically, the results reinforce the importance of careful evaluation and histopathological investigation of persistent intraoral nodules, even when presenting indolent characteristics.

Acknowledgments

None.

Conflict of interests

The authors have no conflicts of interest to declare.

Regulatory Statement / Ethics

This study was conducted in accordance with all the provisions of the local human subject's oversight committee guidelines and policies of: "strengthening the reporting of observational studies in Epidemiology" (STROBE) checklist and statement. This study protocol was reviewed and approved by the Research Ethics Committee of UNIUBE, approval number [83277824.2.0000.5145].

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Authors' contributions

All authors whose names appear on the submission have: 1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; and/or 2) drafted the work or revised it critically for important intellectual content; and/or 3) approved the version to be published; and/or 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

5.8 TABLES

Table 1: Demographic characteristics and histopathological distribution of minor salivary gland neoplasms

		Gender				Skin Color N (%)*		
Category	**Total N (%)**	**Female N (%)**	**Male N (%)**	**Mean Age (SD)**	**Age Range**	**White**	**Non White**	**Untold**
Nature								
Benign Neoplasm	125 (54.6)	91 (72.8)	34 (27.2)	47.1 (± 18.4)	11 - 86	55 (44.0)	56 (44.8)	14 (11.2)
Malignant Neoplasm	104 (45.4)	59 (56.7)	45 (43.3)	52.3 (± 18.9)	13 - 87	48 (46.2)	39 (37.5)	17 (16.3)
Total	**229 (100.0)**	**150 (65.5)**	**79 (34.5)**	**49.3 (± 18.7)**	**11 - 87**	**103 (45.0)**	**95 (41.5)**	**31 (13.5)**
Histopathological Subtypes								
Pleomorphic Adenoma	92 (40.2)	68 (73.9)	24 (26.1)	43.1 (± 18.2)	11 - 86	44 (47.8)	40 (43.5)	8 (8.7)
Mucoepidermoid Carcinoma	34 (14.8)	22 (64.7)	12 (35.3)	41.3 (± 18.1)	13 - 87	16 (47.1)	13 (38.2)	5 (14.7)
Polymorphous Adenocarcinoma	22 (9.6)	14 (63.6)	8 (36.4)	60.7 (± 16.8)	28 - 86	11 (50.0)	9 (40.9)	2 (9.1)
Adenoid Cystic Carcinoma	21 (9.2)	10 (47.6)	11 (52.4)	55.2 (± 15.8)	34 - 86	10 (47.6)	8 (38.1)	3 (14.3)
Salivary Gland Carcinoma NOS	16 (7.0)	7 (43.8)	9 (56.3)	61.1 (± 10.9)	36 - 81	9 (56.3)	3 (18.8)	4 (25.0)

Canalicular Adenoma	12 (5.2)	9 (75.0)	3 (25.0)	63.8 (± 13.9)	34 - 85	4 (33.3)	6 (50.0)	2 (16.7)
Salivary Gland Myoepithelioma	9 (3.9)	5 (55.6)	4 (44.4)	45.1 (± 14.4)	20 - 67	3 (33.3)	6 (66.7)	0 (0.0)
Basal Cell Adenoma	8 (3.5)	7 (87.5)	1 (12.5)	58.0 (± 11.8)	44 - 76	3 (37.5)	2 (25.0)	3 (37.5)
Acinic Cell Carcinoma	4 (1.7)	2 (50.0)	2 (50.0)	37.0 (± 27.2)	17 - 68	1 (25.0)	3 (75.0)	0 (0.0)
Cystadenoma of the Salivary Glands	3 (1.3)	2 (66.7)	1 (33.3)	62.0 (± 5.1)	56 - 65	1 (33.3)	1 (33.3)	1 (33.3)
Hyalinizing Clear Cell Carcinoma	3 (1.3)	1 (33.3)	2 (66.7)	77.0 (± 3.4)	75 - 81	0 (0.0)	1 (33.3)	2 (66.7)
Sebaceous Adenocarcinoma	2 (0.9)	2 (100.0)	0 (0.0)	42.0 (± 19.7)	28 - 56	1 (50.0)	0 (0.0)	1 (50.0)
Mucinous Adenocarcinoma	1 (0.4)	1 (100.0)	0 (0.0)	46	46	0 (0.0)	1 (100.0)	0 (0.0)
Secretory Carcinoma	1 (0.4)	0 (0.0)	1 (100.0)	14	14	0 (0.0)	1 (100.0)	0 (0.0)
Sialolipoma	1 (0.4)	0 (0.0)	1 (100.0)	66	66	0 (0.0)	1 (100.0)	0 (0.0)
Total	**229 (100.0)**	**150 (65.5)**	**79 (34.5)**	**49.3 (± 18.7)**	**11 - 87**	**103 (45.0)**	**95 (41.5)**	**31 (13.5)**

Source: research data

*Categorized according to the Brazilian Institute of Geography and Statistics (IBGE, 2022) classification and grouped into White and Non-White for statistical analysis.

Table 2: Distribution of minor salivary gland neoplasms according to anatomic site and histological subtype

	Anatomic Site								
Minor Salivary Glands Tumors	**Palate N (%)**	**Lip N (%)**	**Buccal Mucosa N (%)**	**Alveolar Ridge N (%)**	**Retromolar N (%)**	**Floor of the Mouth N (%)**	**Oropharynx N (%)**	**Tongue N (%)**	**Maxillary Sinus N (%)**
Histological Subtype									
Benign Neoplasm	**70 (56.6)**	**28 (22.4)**	**14 (11.2)**	**4 (3.2)**	**5 (4.0)**	**3 (2.4)**	**1 (0.8)**	**0 (0.0)**	**0 (0.0)**
Pleomorphic Adenoma	59 (64.1)	12 (13.0)	10 (10.9)	3 (3.3)	4 (4.3)	3 (3.3)	1 (1.1)	0 (0.0)	0 (0.0)
Canalicular Adenoma	1 (8.3)	9 (75.0)	2 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary Gland Myoepithelioma	6 (66.7)	2 (22.2)	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Basal Cell Adenoma	2 (25.0)	4 (50.0)	1 (12.5)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystadenoma of the Salivary Glands	1 (33.3)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sialolipoma	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Malignant Neoplasm	**38 (36.5)**	**7 (6.7)**	**19 (18.3)**	**13 (12.5)**	**12 (11.5)**	**6 (5.8)**	**3 (2.9)**	**5 (4.8)**	**1 (1.0)**
Mucoepidermoid Carcinoma	13 (38.2)	1 (2.9)	6 (17.6)	1 (2.9)	9 (26.5)	3 (8.8)	0 (0.0)	1 (2.9)	0 (0.0)
Polymorphous Adenocarcinoma	11 (50.0)	3 (13.6)	4 (18.2)	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.1)	0 (0.0)
Adenoid Cystic Carcinoma	8 (38.1)	0 (0.0)	4 (19.0)	3 (14.3)	2 (9.5)	1 (4.8)	0 (0.0)	2 (9.5)	1 (4.8)
Salivary Gland Carcinoma NOS	3 (18.8)	1 (6.3)	4 (25.0)	5 (31.3)	0 (0.0)	0 (0.0)	3 (18.8)	0 (0.0)	0 (0.0)
Acinic Cell Carcinoma	2 (50.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Hyalinizing Clear Cell Carcinoma	1 (33.3)	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sebaceous Adenocarcinoma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mucinous Adenocarcinoma	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Secretory Carcinoma	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	**108 (47.2)**	**35 (15.3)**	**33 (14.4)**	**17 (7.4)**	**17 (7.4)**	**9 (3.9)**	**4 (1.7)**	**5 (2.2)**	**1 (0.4)**

Source: research data

Table 3: Symptomatology, time to diagnosis, lesion size, and clinical manifestation of minor salivary gland neoplasms according to histological type

Minor Salivary Glands Tumors	Symptomatology		Time Until Diagnosis (In Months)			Size (cm)			Manifestation	
Histological Subtype	**Yes N (%)**	**No N (%)**	**Mean (SD)**	**Range**	**Untold N (%)**	**Mean (SD)**	**Range**	**Untold N (%)**	**Primary N (%)**	**Recurrent N (%)**
Benign Neoplasm	**10 (8.0)**	**115 (92.0)**	**36.5 (± 51.2)**	**0.2 - 300**	**41 (32.8)**	**2.3 (± 1.7)**	**0.2 - 10**	**2 (1.6)**	**116 (92.8)**	**9 (7.2)**
Pleomorphic Adenoma	7 (7.6)	85 (92.4)	42.6 (± 54.4)	0.5 - 300	28 (30.4)	2.4 (± 1.8)	0.3 - 10	1 (1.1)	86 (93.5)	6 (6.5)
Canalicular Adenoma	0 (0.0)	12 (100.0)	15.5 (± 12.6)	2.0 - 36	5 (41.7)	1.4 (± 0.8)	0.3 - 3.0	0 (0.0)	12 (100.0)	0 (0.0)
Salivary Gland Myoepithelioma	1 (11.1)	8 (88.9)	26.6 (± 41.8)	0.3 - 120	2 (22.2)	2.4 (± 2.3)	0.3 - 7.0	1 (11.1)	7 (77.8)	2 (22.2)
Basal Cell Adenoma	2 (25.0)	6 (75.0)	5.5 (± 4.7)	1.0 - 12	4 (50.0)	1.6 (± 1.2)	0.5 - 4.0	0 (0.0)	7 (87.5)	1 (12.5)
Cystadenoma of the Salivary Glands	0 (0.0)	3 (100.0)	0.2	0.2	2 (66.7)	1.2 (± 0.9)	0.2 - 2.0	0 (0.0)	3 (100.0)	0 (0.0)
Sialolipoma	0 (0.0)	1 (100.0)	12	12	0 (0.0)	3,0	3,0	0 (0.0)	1 (100.0)	0 (0.0)
Malignant Neoplasm	**40 (38.5)**	**64 (61.5)**	**31.9 (± 69.6)**	**0.2 - 480**	**28 (26.9)**	**2.9 (± 2.3)**	**0.2 - 10**	**5 (4.8)**	**95 (91.3)**	**9 (8.7)**
Mucoepidermoid Carcinoma	8 (23.5)	26 (76.5)	35.7 (± 53.6)	0.2 - 180	10 (29.4)	2.2 (± 1.7)	0.5 - 9.0	1 (2.9)	32 (94.1)	2 (5.9)
Polymorphous Adenocarcinoma	10 (45.5)	12 (54.5)	38.8 (± 66.9)	1.0 - 240	5 (22.7)	3.2 (± 2.6)	0.2 - 10	0 (0.0)	20 (90.9)	2 (9.1)

Adenoid Cystic Carcinoma	13 (61.9)	8 (38.1)	10.5 (± 7.7)	2.0 - 24	5 (23.8)	3.8 (± 2.9)	1.0 - 10	1 (4.8)	18 (85.7)	3 (14.3)
Salivary Gland Carcinoma NOS	4 (25.0)	12 (75.0)	14.9 (± 28.6)	0.7 - 96	5 (31.3)	2.6 (± 1.6)	0.6 - 6.0	2 (12.5)	14 (87.5)	2 (12.5)
Acinic Cell Carcinoma	3 (75.0)	1 (25.0)	27.3 (± 20.0)	8.0 - 48	1 (25.0)	1.7 (± 1.5)	1.0 - 4.0	0 (0.0)	4 (100.0)	0 (0.0)
Hyalinizing Clear Cell Carcinoma	0 (0.0)	3 (100.0)	480	480	2 (66.7)	5.0 (± 0.0)	5.0 - 5.0	1 (33.3)	3 (100.0)	0 (0.0)
Sebaceous Adenocarcinoma	2 (100.0)	0 (0.0)	3.5 (± 0.7)	3.0 - 4.0	0 (0.0)	1.75 (1.7)	0.5 - 3.0	0 (0.0)	2 (100.0)	0 (0.0)
Mucinous Adenocarcinoma	0 (0.0)	1 (100.0)	2	2	0 (0.0)	3,0	3,0	0 (0.0)	1 (100.0)	0 (0.0)
Secretory Carcinoma	0 (0.0)	1 (100.0)	3	3	0 (0.0)	3,0	3,0	0 (0.0)	1 (100.0)	0 (0.0)
Total	**50 (21.8)**	**179 (78.2)**	**34.1 (± 60.3)**	**0.2 - 480**	**69 (30.1)**	**2.5 (± 2.0)**	**0.2 - 10**	**7 (3.1)**	**211 (92.1)**	**18 (7.9)**

Source: research data

Table 4: Clinical description of minor salivary gland neoplasms according to histological type

	Clinical Description										
Minor Salivary Glands Tumors	**Nodule**			**Ulcer**			**Lesion Color**				
Histological Subtype	**Yes N (%)**	**No N (%)**	**Untold N (%)**	**Yes N (%)**	**No N (%)**	**Untold N (%)**	**Normochromic N (%)**	**Erythematous N (%)**	**Whitish N (%)**	**Yellowish N (%)**	**Untold N (%)**
Benign Neoplasm	**114 (91.2)**	**5 (4.0)**	**6 (4.8)**	**5 (4.0)**	**114 (91.2)**	**6 (4.8)**	**69 (55.2)**	**25 (20.0)**	**10 (8.0)**	**6 (4.8)**	**15 (12.0)**
Pleomorphic Adenoma	86 (93.5)	2 (2.2)	4 (4.3)	3 (3.3)	85 (92.4)	4 (4.3)	55 (59.8)	14 (15.2)	7 (7.6)	5 (5.4)	11 (12.0)
Canalicular Adenoma	12 (100.0)	0 (0.0)	0 (0.0)	1 (8.3)	11 (91.7)	0 (0.0)	3 (25.0)	4 (33.3)	1 (8.3)	1 (8.3)	3 (25.0)
Salivary Gland Myoepithelioma	9 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)	0 (0.0)	6 (66.7)	3 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
Basal Cell Adenoma	7 (87.5)	1 (12.5)	0 (0.0)	0 (0.0)	8 (100.0)	0 (0.0)	4 (50.0)	2 (25.0)	1 (12.5)	0 (0.0)	1 (12.5)
Cystadenoma of the Salivary Glands	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)
Sialolipoma	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Malignant Neoplasm	**79 (76.0)**	**19 (18.3)**	**6 (5.8)**	**19 (18.3)**	**79 (76.0)**	**6 (5.8)**	**36 (34.6)**	**36 (34.6)**	**8 (7.7)**	**2 (1.9)**	**22 (21.2)**
Mucoepidermoid Carcinoma	30 (88.2)	2 (5.9)	2 (5.9)	6 (17.6)	26 (76.5)	2 (5.9)	14 (41.2)	11 (32.4)	4 (11.8)	0 (0.0)	5 (14.7)

Polymorphous Adenocarcinoma	17 (77.3)	5 (22.7)	0 (0.0)	5 (22.7)	16 (72.7)	1 (4.5)	5 (22.7)	10 (45.5)	1 (4.5)	0 (0.0)	6 (27.3)
Adenoid Cystic Carcinoma	19 (90.5)	1 (4.8)	1 (4.8)	4 (19.0)	16 (76.2)	1 (4.8)	6 (28.6)	7 (33.3)	2 (9.5)	2 (9.5)	4 (19.0)
Salivary Gland Carcinoma NOS	13 (81.3)	1 (6.3)	2 (12.5)	2 (12.5)	12 (75.0)	2 (12.5)	8 (50.0)	4 (25.0)	1 (6.3)	0 (0.0)	3 (18.8)
Acinic Cell Carcinoma	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (75.0)	1 (25.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)
Hyalinizing Clear Cell Carcinoma	2 (66.7)	0 (0.0)	1 (33.3)	0 (0.0)	2 (66.7)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)
Sebaceous Adenocarcinoma	2 (100.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mucinous Adenocarcinoma	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Secretory Carcinoma	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	**193 (84.3)**	**24 (10.5)**	**12 (5.2)**	**24 (10.5)**	**193 (84.3)**	**12 (5.2)**	**105 (45.9)**	**61 (26.6)**	**18 (7.9)**	**8 (3.5)**	**37 (16.2)**

Source: research data

Table 5: Association between tumor nature and clinicopathological variables based on Fisher's exact test.

Nature	Gender			p-value (Fisher)
	Female	**Male**	**Not reported**	
Benign	91	34	0	***0,0123***
Malignant	59	45	0	
	Age			
	Young and Adults	**Elderly**	**Not reported**	
Benign	89	33	3	0,083
Malignant	61	38	5	
	Skin Color*			
	White	**Non-White**	**Not reported**	
Benign	55	56	14	0,475
Malignant	48	39	17	
	Anatomic Site			
	Palate	**Other sites**	**Not reported**	
Benign	70	55	0	***0,0036***
Malignant	38	66	0	
	Evolution Time			
	< 12 Months	**≥ 12 Months**	**Not reported**	
Benign	27	58	40	***0,0102***
Malignant	40	36	28	
	Size			
	< 2 cm	**≥ 2 cm**	**Not reported**	
Benign	51	72	2	0,582
Malignant	37	62	5	
	Symptomatology			
	Asymptomatic	**Symptomatic**	**Not reported**	
Benign	115	10	0	***< 0.0001***
Malignant	64	40	0	
	Elementary Lesion			
	Nodule	**Ulcer**	**Not reported**	
Benign	114	5	6	***0,0004***
Malignant	79	19	6	
	Elementary Lesion			
	Nodule (Yes)	**Nodule (No)**	**Not reported**	
Benign	114	5	6	***0,0004***
Malignant	79	19	6	

	Elementary Lesion			
	Ulcer (Yes)	**Ulcer (No)**	**Not reported**	
Benign	5	114	6	***0,0004***
Malignant	19	79	6	
	Base			
	Sessile	**Pedunculated**	**Not reported**	
Benign	33	7	85	0,1587
Malignant	34	2	68	
	Borders			
	Well defined	**Poorly Defined**	**Not reported**	
Benign	14	3	108	0,0526
Malignant	1	3	100	
	Color			
	Normochromic	**Other**	**Not reported**	
Benign	69	41	15	***0,0126***
Malignant	36	46	22	
	Clinical Presentation			
	Primary	**Secondary**	**Not reported**	
Benign	116	9	0	0,8064
Malignant	95	9	0	
	Treatment			
	Incisional B.	**Excisional B.**	**Not reported**	
Benign	32	88	5	***< 0.0001***
Malignant	56	40	8	
	Surgical Margins (Excisional B.)			
	Free	**Compromised**	**Not Computed (Incisional B. and Others)**	
Benign	66	21	38	***0,0211***
Malignant	21	18	65	

Source: research data

*Categorized according to the Brazilian Institute of Geography and Statistics (IBGE, 2022) classification and grouped into White and Non-White for statistical analysis.

TABLE 6 Distribution of minor salivary gland tumors in Brazil

							Nature		Gender			Skin color		Most frequent site (minor SGNs)	Three most frequent histological types		
Author	**Year**	**Region**	**Number of centers**	**Sample (MSGNs)**	**Total (SGNs)**	**Total cases**	**Benign Tumors N (%)**	**Malignant tumors N (%)**	**Female N (%)**	**Male N (%)**	**Mean age**	**White N (%)**	**Non-white N (%)**		**1st (N, %)**	**2st (N, %)**	**3st (N, %)**
Loyola *et al.*	1995	Southeast	1	164 (100.0)	164	-	102 (62.0)	62 (38.0)	90 (56.0)	70 (44.0)	41.5	NI	NI	Palate: N NI (73.0)	PA 87 (53.0)	MEC 28 (17.0)	ACC 22 (13.0)
*Vargas *et al.*	2002	Southeast	2	6 (5.0)	124	-	2 (33.3)	4 (66.6)	I MSG	I MSG	I MSG	NI	NI	NI	MEC 3 (50.0)	PA 2 (33.3)	ACC 1 (16.7)
*Santos *et al.*	2003	Southeast	1	11 (9.2)	119 (0.06)	205.967	I MSG	I MSG	I MSG	I MSG	I MSG	NI	NI	NI	**PA 71 (59.7)	**ACC 12 (10.0)	**MEC 11 (9.3)
*Barbosa *et al.*	2005	Northeast	2	7 (24.1)	29 (3.17)	914	0 (0.0)	7 (100.0)	I MSG	I MSG	I MSG	NI	NI	NI	ACC 5 (71.4)	NOS 1 (14.3)	AcCC 1 (14.3)
*Ito *et al.*	2005	South	1	113 (22.8)	496	-	42 (37.2)	71 (62.8)	I MSG	I MSG	I MSG	NI	NI	Palate: 76 (67.0)	PA 38 (33.6)	ACC 28 (24.8)	MEC 25 (22.1)
*Lima *et al.*	2005	Northeast	1	46 (18.8)	245 (0.15)	162.312	24 (52.2)	22 (47.8)	I MSG	I MSG	I MSG	I MSG	I MSG	NI	PA 23 (95.8)	ACC 8 (36.8)	MEC 6 (27.3)
*Loiola *et al.*	2009	Northeast	1	35 (15.1)	232	-	13 (7.3)	22 (40.7)	I MSG	I MSG	I MSG	NI	NI	NI	PA 13 (37.1)	ACC 9 (25.7)	MEC 8 (22.9)
*Oliveira *et al.*	2009	Northeast	1	87 (14.5)	599	-	37 (8.0)	50 (40.0)	53 (60.9)	34 (39.1)	48	NI	NI	Palate: 61 (70.1)	PA 32 (36.8)	MEC 16 (18.4)	ACC 16 (18.4)
*Agripino *et al.*	2010	Northeast	1	91 (50.3)	181	-	I MSG	I MSG	39 (42.9)	52 (57.1)	I MSG	NI	NI	NI	**PA 31 (17.1)	**NOS 6 (3.3)	**ACC 5 (2.8)
Nóbrega *et al.*	2010	Northeast	1	83 (100.0)	83 (0.90)	9.222	43 (51.8)	40 (48.2)	58 (69.9)	25 (30.1)	44	NI	NI	Palate: 36 (43.4)	PA 32 (38.6)	MEC 15 (18.1)	ACC 11 (13.3)

*Morais *et al.*	2011	Northeast	1	37 (12.2)	303 (0.48)	62.930	11 (29.7)	26 (70.3)	26 (70.3)	11 (29.7)	I MSG	NI	NI	NI	MEC 17 (46.0)	PA 9 (24.3)	ACC 3 (8.1)
*Fonseca *et al.*	2012	Southeast and South	2	156 (31.6)	493	-	81 (51.9)	75 (48.1)	I MSG	I MSG	I MSG	NI	NI	Palate: 95 (60.9)	PA 81 (51.9)	MEC 26 (16.7)	PAC 13 (10.3)
*Melo *et al.*	2012	Northeast	1	34 (25.4)	134	-	16 (47.1)	18 (52.9)	I MSG	I MSG	I MSG	NI	NI	NI	PA 16 (47.1)	ACC 14 (41.2)	PAC 2 (5.9)
*Lima *et al.*	2015	Northeast	1	35 (70.0)	50	-	I MSG	I MSG	I MSG	I MSG	I MSG	NI	NI	Palate: 19 (54.3)	PA 31 (62.0)	MEC 7 (14.0)	ACC 5 (10.0)
Abrahão *et al.*	2016	Southeast	2	170 (100.0)	170	-	89 (52.0)	81 (48.0)	104 (61.0)	66 (39.0)	51 (± 19.0)	NI	NI	Palate: 95 (56.0)	PA 75 (44.0)	MEC 23 (14.0)	PAC 21 (12.0)
Sarmento *et al.*	2016	Northeast	1	37 (100.0)	37	-	11 (29.7)	26 (70.3)	26 (70.3)	11 (29.7)	NI	NI	NI	Palate: 25 (67.6)	MEC 17 (45.9)	PA 9 (24.4)	PAC 5 (13.5)
*Vasconc elos *et al.*	2016	South	1	28 (25.7)	109 (5.03)	2.168	18 (64.3)	10 (35.7)	I MSG	I MSG	I MSG	NI	NI	Palate: 16 (57.1)	PA 18 (64.3)	ACC 8 (28.6)	AcCC 2 (7.1)
*Barin *et al.*	2017	South	1	10 (24.4)	41(59.4)	69	I MSG	I MSG	I MSG	I MSG	I MSG	NI	NI	Palate: 3 (30.0)	**PA 15 (36.6)	**NOS 4 (9.8)	**WT 2 (4.9)
*Silva *et al.*	2018	Northeast and Southeast	5	1114 (48.6)	2.292 (2.59)	88.430	515 (46.2)	599 (53.8)	I MSG	I MSG	I MSG	I MSG	I MSG	Palate: 631 (56.6)	PA 382 (34.3)	MEC 195 (17.5)	PAC 144 (12.9)
*Reinhei mer *et al.*	2019	South	2	36 (29.0)	124 (0.10)	129.21 1	22 (61.1)	14 (38.9)	I MSG	I MSG	I MSG	NI	NI	Palate: 22 (61.1)	PA 18 (50.0)	MEC 5 (13.9)	ACC 4 (11.1)
Viveiros *et al.*	2019	Southeast	1	687 (100.0)	687 (0.95)	72.286	342 (49.8)	345 (50.2)	450 (65.5)	237 (34.5)	48.4	NI	NI	Palate: 364 (53.0)	PA 250 (36.4)	CME 116 (16.9)	ACC 72 (10.5)
*Cunha *et al.*	2020	Northeast	4	159 (27.0)	588	-	113 (71.1)	46 (28.9)	I MSG	I MSG	I MSG	NI	NI	Palate: 101 (63.5)	PA 101 (63.5)	MEC 17 (10.7)	ACC 9 (5.7)
Bruzinga *et al.*	2021	Southeast	2	480 (100.0)	480 (0.90)	53.578	272 (56.7)	147 (30.7)	307 (64.0)	173 (36.0)	45.32 (± 18.4)	NI	NI	Palate: 336 (70.1)	PA 245 (51.1)	MEC 70 (14.6)	ACC 43 (8.9)

*Rodrigues *et al.*	2022	Northeast	1	62 (72.1)	86 (0.90)	9.613	I MSG	I MSG	I MSG	I MSG	I MSG	I MSG	I MSG	Palate: 37 (59.7)	PA 49 (57.0)	MEC 23 (26.7)	ACC 14 (16.3)
*Brazão *et al.*	2023	South	1	7 (20.0)	35 (0.09)	40.555	7 (100.0)	0 (0.0)	I MSG	I MSG	I MSG	I MSG	I MSG	Palate: 7 (100.0)	**PA 31 (89.0)	**MIO 3 (9.0)	**WT 1 (3.0)
Present study	2025	Southeast	2	229 (66.6)	344 (1.4)	25168	125 (54.6)	104 (45.4)	150 (65.5)	79 (34.5)	49,3 (± 18.7)	103 (45.0)	95 (41.5)	Palate: 108 (47.2)	PA 92 (40.2)	MEC 34 (14.8)	PAC 22 (9.6)

Abbreviations: n, absolute frequency; %, relative frequency; ACC, adenoid cystic carcinoma; AcCC, acinic cell carcinoma; I MSG, Including Major salivary glands; MSG, Major salivary glands; MSGNs, Minor Salivary Gland Neoplasms; NI, not informed; PA, pleomorphic adenoma; SGNs, Salivary Gland Neoplasms; WT, Warthin's tumor; MEC, mucoepidermoid carcinoma; PAC, polymorphous adenocarcinoma.

*Adapted data - information of only minor salivary glands tumors.

** Cases of major salivary glands were considered, since the study did not differentiate them from minor salivary glands.

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6 CONCLUSÃO

O presente estudo analisou retrospectivamente o perfil clinicopatológico das neoplasias de glândulas salivares menores diagnosticadas em dois serviços de Patologia Oral do Triângulo Mineiro, identificando 229 casos entre 25.168 laudos anatomopatológicos. Esses achados evidenciam a raridade dessas lesões no contexto das patologias orais, mas também sua expressiva representatividade entre os tumores de glândulas salivares.

Observou-se predominância de neoplasias benignas, com destaque para o Adenoma Pleomórfico, seguido pelo Carcinoma Mucoepidermoide e pelo Adenocarcinoma Polimorfo. Houve maior acometimento do sexo feminino, média etária próxima à quinta década de vida e predileção pelo palato, em concordância com a literatura.

Do ponto de vista clínico, as lesões caracterizaram-se principalmente por crescimento nodular, evolução lenta e ausência de sintomas, o que pode dificultar o diagnóstico precoce. Entretanto, a análise comparativa evidenciou associação significativa entre malignidade e características como sexo masculino, localização extrapalatina, menor tempo de evolução, presença de sintomas, ulceração e coloração não normocrômica.

Dessa forma, os resultados reforçam a importância da avaliação clínica criteriosa de lesões nodulares persistentes da cavidade oral, associada à confirmação histopatológica, além de contribuírem para o melhor entendimento do perfil epidemiológico dessas neoplasias na população brasileira.

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* As referências desta seção foram elaboradas conforme as normas da Associação Brasileira de Normas Técnicas (ABNT), seguindo a NBR 6023:2018.

ANEXOS

ANEXO A – APROVAÇÃO NO CEP

UNIVERSIDADE DE UBERABA - UNIUBE

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: NEOPLASIAS DE GLÂNDULAS SALIVARES MENORES: ESTUDO OBSERVACIONAL RETROSPECTIVO E IMUNOHISTOQUÍMICO
Pesquisador: João Paulo Silva Servato
Área Temática:
Versão: 1
CAAE: 83277824.2.0000.5145
Instituição Proponente: SOCIEDADE EDUCACIONAL UBERABENSE
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 7.101.438

Apresentação do Projeto:
Projeto de pesquisa coordenado por João Paulo Silva Servato, com colaboração de Marcelo Sivieri de Araújo e Pedro Henrique Silva de Gracia.
"A região maxilo facial é organizada em estruturas anatômicas, formando um sistema. Dentre as estruturas, tem-se as Glândulas Salivares, as quais desempenham funções importantes, e são divididas em Glândulas Salivares Maiores e Menores. Elas estão susceptíveis ao desenvolvimento de doenças, inclusive as neoplásicas, podendo ser de caráter benigno ou maligno. Atingem em sua maioria a Glândula Parótida, mas também são observados casos nas Glândulas Submandibulares, Sublinguais e nas Glândulas Salivares Menores, as quais serão objeto de estudo desta pesquisa. As lesões são de caráter heterogêneo, com histologia e morfologia complexas, o que dificulta a categorização dessas lesões, uma vez que no início do desenvolvimento da doença, elas são muito parecidas umas com as outras."
"Diante do exposto, o objetivo desta pesquisa se dá em descrever e analisar os casos diagnosticados retrospectivamente como Neoplasias intraorais de Glândula Salivar Menor, procedentes do Serviço de Estomatologia/Patologia Oral da Universidade Federal de Uberlândia/UFU (1978-2024) e da Universidade de Uberaba/UNIUBE (1999-2024). Além do objetivo anterior, este trabalho busca também avaliar a imunoexpressão de marcadores de proliferação e de apoptoses em amostras de lesões benignas e malignas. A técnica a ser utilizada para identificação da expressão das proteínas ligados à proliferação (Ki-67) e

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Continuação do Parecer: 7.101.438

Folha de Rosto	folha_de_rosto.pdf	11/09/2024 09:11:57	João Paulo Silva Servato	Aceito
Projeto Detalhado / Brochura Investigador	4_Projeto_CEP.pdf	10/09/2024 11:36:44	João Paulo Silva Servato	Aceito
Solicitação Assinada pelo Pesquisador Responsável	6_Carta_de_encaminhamento.pdf	10/09/2024 11:31:43	João Paulo Silva Servato	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	5_Justificativa_para_dispensa_do_Termo_de_Consentimento_Livre_e_Esclarecido.pdf	10/09/2024 11:31:29	João Paulo Silva Servato	Aceito
Declaração de Pesquisadores	3_Termo_de_compromisso_para_uso_de_dados_arquivo.pdf	10/09/2024 11:31:12	João Paulo Silva Servato	Aceito
Declaração de Pesquisadores	3_Outros_Termo_de_Responsabilidade.pdf	10/09/2024 11:31:04	João Paulo Silva Servato	Aceito
Declaração de Pesquisadores	2_Declaracao_pesquisador.pdf	10/09/2024 11:30:46	João Paulo Silva Servato	Aceito
Declaração de Instituição e Infraestrutura	1_Autorizacao_UNIUBE.pdf	10/09/2024 11:30:38	João Paulo Silva Servato	Aceito
Declaração de Instituição e Infraestrutura	1_Autorizacao_UFU.pdf	10/09/2024 11:30:29	João Paulo Silva Servato	Aceito
Declaração de Instituição e Infraestrutura	1_Autorizacao_PGV.pdf	10/09/2024 11:30:23	João Paulo Silva Servato	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

UBERABA, 25 de Setembro de 2024

Assinado por:
NELSON RANNIERI TIRONE
(Coordenador(a))

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ANEXO B – MEDICINA ORAL PATOLOGÍA ORAL Y CIRURGIA BUCAL – EISSN: 1698-6946

INSTRUCTIONS FOR AUTHORS - Medicina Oral Patologia Oral y Cirugia Bucal - eISSN: 1698-6946

Medicina Oral Patologia Oral y Cirugia Bucal is a multidisciplinary and international journal dedicated to research about "Oral Medicine-Pathology, Oral Surgery and systemic diseases with oral manifestations" with the latest findings from basic and clinical studies.

The main focus areas for articles submitted to the journal are:
1. Digital dentistry and artificial intelligence
2. Biomarkers in Dentistry
3. Oral microbiome
4. Oral manifestations of systemic diseases
5. Implantology, biomaterials, and guided surgery
6. New diagnostic methods and treatments in Oral Medicine-Pathology, Oral Surgery.

Medicina Oral Patologia Oral y Cirugia Bucal is indexed and abstracted in: Science Citation Index Expanded, Journal Citation Reports, Index Medicus, MEDLINE, PubMed, Scopus, Embase and Emcare, Indice Médico Español, IBECS, Dialnet, Latindex

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ARTICLE SUBMISSION
Articles may only be submitted through our website and in ENGLISH. Log on to our website, and we will send you a username and PASSWORD to submit the article.

For submitting NEW OR MODIFIED MANUSCRIPTS, the description of the process is:
1. Log in to http://www.medoral.es
2. Click on "Submit a manuscript" for submitting a NEW articles. Click on "Submissions needing revision" for submitting a MODIFIED article.
3. Upload a word document entitled: "**Letter to the Editor**". (We do not admit word in format .doc . You must submit a .docx document) If this is a modification of a previously submitted article, this letter should include the answers to ALL the reviewer´s comments.
4. Include a separate **Word document** entitled: "**Manuscript**". (We do not admit word in format .doc. You must submit a .docx document) You may upload a **.docx** file for the manuscript. If you create a **.docx** file, make sure that all the tables created are included with the correct format, spacing, and width in the **.docx** document. Don't try to create a document with a table width higher than the document width, or insert a table with a negative left/right spacing. It may crash at the summary step.

The **manuscript** must include the following items:
- Title of the article
- Authors (First and last name, ORCID). The maximum number of authors of an article will be 10. More authors will be allowed only in exceptional situations for multicenter research studies accredited under an official research project, with the reference number and the institution that approved it.
- Contact address for the corresponding author
- Abstract, containing 150-300 words, ALWAYS structured as: Background, Materials and Methods, Results, Conclusions.
- Running title
- Key words
- Abstract
- Text of the article
- References
- Insert ALL TABLES in the main manuscript. Each table in one page
- Figure legends
  Please note that tables must be in portrait orientation; we do not accept landscape tables.
  DO NOT INCLUDE THE FIGURES IN THE MAIN MANUSCRIPT

5. **Upload figures**, one at a time. Do not include figures in the manuscript document. Figures must be at least ***900 × 600 pixels*** and in ***JPEG (.jpg)*** format; file size must be less than ***5 MB***. Please convert your figures to JPEG format ***without compression in RGB, not CMYK***. All figures that do not correspond to these requirements will be rejected.

   If you are resubmitting a modified document in response to the reviewers' comments, all changes MUST be highlighted in RED.

All accepted articles of this ONLINE VERSION will be published in ENGLISH and included in the SCIENCE CITATION INDEX EXPANDED (since 2008), JOURNAL CITATION REPORTS (since 2008), INDEX MEDICUS, MEDLINE, PUBMED, SCOPUS, EMCARE, EMBASE, INDICE MEDICO ESPAÑOL.

Articles will normally be included in one of the different journal sections. Authors should indicate the section in which they wish their article to be included, although the Editor may change this upon advice from reviewers. Articles received will always undergo revision by a committee of experts *(peer review process - anonymous)*. Authors are ***RESPONSIBLE*** for all opinions, results, and conclusions contained in articles, which will not necessarily be shared by the journal's Editor and reviewers. All accepted articles become the property of Medicina Oral S.L., and their date of reception and acceptance will be reflected; thus, their subsequent publication in other media is not allowed without written permission by the Editor. Authors will transfer IN WRITING the copyright of their contributions to Medicina Oral S.L.

TYPES OFARTICLES
Medicina Oral Patologia Oral y Cirugia Bucal no longer ADMITS CASE REPORTS.

We admit:
1. Original Articles
Analytical investigations such as cross-sectional surveys, case-control studies, cohort studies, and controlled clinical trials will be recommended for publication. For clinical trials, authors must specify the legal permissions obtained.

1.1.Title. Clear, precise, and specific. Must reflect the content of the study.

1.2. Abstract
A brief summary of the study. Includes: objective, methods, main results, and conclusions.
Structured (with subheadings).
1.3. Keywords
Between 3 and 6 relevant terms.
Facilitate indexing in databases.
1.4. Short title
1.5. Introduction
Context of the problem.
Brief review of the relevant literature.
Rationale for the study.
Objective(s) or hypothesis.
1.6. Materials and Methods
Study design (experimental, observational, etc.).
Population and sample.
Variables and how they were measured.
Procedures.
Statistical analysis.
Ethical considerations.
1.7. Results
Objective presentation of findings.
Use of tables and figures.
No interpretation (data only).
1.8. Discussion
Interpretation of the results.
Comparison with previous studies.
Implications of the study.
Limitations.
Future lines of research.
1.9. Conclusions
Summary of the main findings.
Addressing the stated objective.
1.10. References
Sources cited in the text.
Format according to the journal (Vancouver).

Articles should not exceed 12 pages (excluding the references) in DIN A4 format, 30 lines per page. No more than four figures and four tables should be included; up to 30 references.

2. Systematic Reviews / Meta-analyses

Articles of special interest and those entailing an update on any of the topics identified as subjects for this journal will be accepted.

2.1. Title and Abstract
It must indicate that it is a systematic review and/or meta-analysis. The abstract typically includes: objective, methods, main results, and conclusions.
2.2. Introduction
Context of the research problem.
Justification for the meta-analysis (why it is necessary).
Objective(s) or research question(s) (in PICO format).
2.3. Methods
This is the most important section due to its rigor and reproducibility.
a) Search strategy
Databases used (PubMed, Scopus, etc.).
Keywords and search terms.
Search dates.
b) Inclusion and exclusion criteria
Types of studies.
Population, intervention, comparator, outcomes.
c) Study selection
Screening process (PRISMA-style flowchart).
d) Data extraction
What data were collected and how.
e) Quality assessment or risk of bias
Tools used (e.g., Cochrane Risk of Bias).
f) Statistical analysis
Type of model (fixed or random effects).
Effect measures (OR, RR, Cohen's d, etc.).
Heterogeneity (I^2).
Sensitivity or subgroup analysis.
Assessment of publication bias (e.g., funnel plot).
2.4. Results
Number of included studies.
Study characteristics.
Quantitative results (forest plots).
Observed heterogeneity.
Results of additional analyses.
2.5. Discussion
Interpretation of results.
Comparison with previous literature.
Clinical or theoretical implications.
Limitations of the meta-analysis.
Possible biases.
2.6. Conclusions
Clear summary of the main findings.
Practical or scientific relevance.
2.7. Other important sections
Funding and conflicts of interest.
Protocol registration (e.g., PROSPERO).
Supplementary material (if applicable).

They should not exceed 14 pages (excluding the references) in DIN A-4 format, with 30 lines per page. They should contain a maximum of four figures and four tables per article; up to 60 references.

REFERENCES

References should be numbered consecutively in order of appearance in the text of the manuscript, cited in square **brackets** in the text. Do not use parentheses or superscripts.
Example: [1] or [1-3] or [1,4-8]
At the end of the document, all references should appear in a numbered list, one after the other, in Vancouver format

Examples of Vancouver References

- *Journal Article*: Author Surname Initials. Title of article. Journal Name (abbreviated). Year Month Day;Volume(Issue):pages.
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- *Book*: Author Surname Initials. Title of book. Edition. Place of publication: Publisher; Year.
  Example: 2. Doe J. Title of book. 2nd ed. London: Publisher; 2025.
- *Website*: Author/Organization. Title of page [Internet]. Place of publication: Publisher; Year [cited Year Month Day]. Available from: URL.

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Statement of Informed Consent

Patients have a right to privacy that should not be infringed without informed consent. Identifying information, including patients' names, initials, or hospital numbers, should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that an identifiable patient be shown the manuscript to be published.

Authors should inform patients if any potentially identifiable material could be accessible via the Internet after publication. Identifying details should be omitted if they are not essential. Complete anonymity is difficult to achieve, but informed consent should be obtained if there is any doubt. For example, masking the eye area in patient photographs is insufficient for protecting anonymity. If identifying features are altered to safeguard anonymity, such as in genetic pedigrees, authors should ensure that these changes do not distort scientific meaning, and editors should note this.

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This journal adheres to the ethical guidelines. All authors must certify that the submitted article has been evaluated by an authorized and recognized Ethical Committee.

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AT THE END OF THE MANUSCRIPT, all submissions to the Journal of Clinical and Experimental Dentistry must include:

1. **Conflict of interest**

Authors must disclose all relationships or interests that could influence or bias the work.

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A conflict of interest exists if authors or their institutions have financial or personal relationships with other people or organizations that could inappropriately influence (bias) their actions.

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All submissions to the Journal of Clinical and Experimental Dentistry must include disclosure of all relationships that could be viewed as presenting a potential conflict of interest.

All authors are required to provide a signed statement of their conflicts of interest as part of the author statement form:

https://www.medicinaoral.com/conflict_med.htm

2. **Ethics.** Under the subheading Ethics, the ethics committee approval with the reference number.
3. **Source of Funding**. Under a subheading of Source of Funding. If funding is not available, disclose it.
4. **Authors' contributions.** Under a subheading of Authors' contributions.

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