***Systematic Review***

**ORAL SEBACEOUS CARCINOMA – A SYSTEMATIC REVIEW**

 **ABSTRACT –**

**Introduction:** Sebaceous carcinoma is predominantly known as a cutaneous malignancy, most commonly arising in the periocular region. It is locally aggressive and has risk of metastasis. occurrence in the oral cavity is exceptionally rare, making it a diagnostic challenge for clinicians and pathologists. Furthermore, recognition of intraoral sebaceous carcinoma is important as it may be associated with genetic syndromes such as Muir-Torre syndrome, which has broader implications for patient management and family screening. Therefore, awareness of this rare entity in the oral cavity is crucial for timely diagnosis, appropriate therapy, and comprehensive patient care. **Objectives:** To know demographics, Clinical and histopathological features, differential diagnosis, treatment and patient outcomes in oral sebaceous carcinoma. **Methods:** Case reports and case series of Oral sebaceous carcinoma were retrieved by a systematic search of 3 electronic database to meet the following inclusion criteria- 1)Case reports and case series on patients with intraoral sebaseous carcinoma from 2000-20242) Articles published in English 3)Case reports and case series , Case reports and case series with review between 2000-2024.Reference checks of the cases identified were also made to help snowballing or networking of the cases. All the required data is extracted from the 13 selected cases. **Results:** The search strategy retrieved 1894 articles. Assessment of the full text was done for 123 articles, but 13 were included. The total of 13 case reports included was, most of them male with mean age 60 years old. n majority of the studies the region affected was upper or lower lip, followed by tongue and palate. linically on extra oral examination the lesion appeared as markedly ulcerated, exophytic, irregularly shaped, indurated mass varying in dimensions. The most common diagnosis arrived at was Sebaceous carcinoma of the oral region. **Conclusion:** Oral sebaceous carcinoma is an extremely rare and aggressive malignancy with a potential for local recurrence and distant metastasis. Regular follow-up is essential to monitor for recurrence or metastasis. Increased awareness among clinicians and pathologists for oral occurrence of sebaceous carcinoma can aid in improving prognosis through timely intervention.

**KEYWORDS – oral sebaceous carcinoma, oral cavity, sebaceous glands**

**Introduction**

Sebaceous carcinoma (SC) is a rare and aggressive cutaneous malignancy, with fewer than 400 cases reported in the literature to date. The first documented case was first described by Allaire in 1891¹. According to the World Health Organization (WHO), sebaceous carcinoma is defined as “a malignant tumor composed of sebaceous cells of varying maturity that are arranged in sheets and/or nests with different degrees of pleomorphism, nuclear atypia, and invasiveness”². This tumor originates from sebaceous glands in the skin and, therefore, can develop anywhere on the body where these glands are present.

Sebaceous carcinoma is classified into two subtypes: ocular and extraocular³. Ocular SC is the third most common malignancy of the eyelids, with most cases originating from the meibomian glands. Extraocular SC accounts for approximately 20% of all cases and typically involves the head and neck region—particularly the scalp, face, parotid gland, buccal mucosa, and tongue³. Among extraocular, non-cutaneous sebaceous carcinoma most commonly involves the major salivary glands⁴.

The first reported case of intraoral (IO) SC was described by Damm et al. in 1991, marking the earliest known instance in English-language literature of sebaceous carcinoma presenting as an intraoral tumor⁸. Although sebaceous adenomas have been documented in the oral cavity, oral sebaceous carcinomas remain extremely rare⁵. Primary SC of the oral cavity is thought to arise from Fordyce granules or from salivary gland elements⁶. Fordyce granules—ectopic sebaceous glands found in about 80% of adults—are considered a normal anatomical variant⁶,⁷. Clinically, they present as asymptomatic, small yellow-white papules on the oral mucosa, with common sites including the buccal mucosa and upper lip⁸. Rarely, these glands may undergo neoplastic transformation, giving rise to sebaceous neoplasms. Oral sebaceous carcinoma often presents as a non-encapsulated, asymptomatic nodule, and can be mistaken for more common benign lesions, which may delays in diagnosis and treatment⁹.

Although the exact etiology of SC remains unclear, several risk factors have been associated with its development. Inherited genetic mutations, particularly those associated with Muir–Torre Syndrome (a variant of Lynch syndrome), are linked to sebaceous carcinoma¹⁰. Additional contributing risk factors include long-term ultraviolet (UV) exposure, immunosuppression, and viral infections¹⁰,¹¹. These genetic alterations often affect DNA mismatch repair genes (*MSH2*, *MSH6*, *MLH1*), leading to microsatellite instability¹¹. Sebaceous Carcinoma most commonly typically affects in middle-aged to elderly individuals, with a mean age of 65 years (range: 9–93 years), and does not demonstrate significant gender predilection¹².

SC is recognized for its aggressive behavior , with the potential for local invasion and distant metastasis¹⁰. Therefore, early detection is essential for effective management. Accurate staging using the TNM system is essential for assesing the extent of the disease, guiding treatment, and providing prognostic information¹³,¹⁴. Due to the absence of standardized imaging protocols, histopathological evaluation of biopsied or excised lesions remains the most reliable diagnostic method. Histologically, SC is part of the sebaceous neoplasm spectrum, which also includes sebaceous adenoma and basal cell carcinoma with sebaceous differentiation¹⁵. SC typically demonstrates well-circumscribed lobules of neoplastic sebaceous cells with eosinophilic cytoplasm and marked atypia. Cytologic features include nuclear pleomorphism and frequent mitotic figures, with occasional foamy or glassy cytoplasm¹⁶,¹⁷.

Optimal treatment involves local surgical excision with clear margins. A 5 mm margin is generally recommended to prevent local recurrence¹⁹. In cases of ocular Sebaceous Carcinoma, regional neck dissection or sentinel lymph node biopsy may be indicated²⁰. The role of adjuvant radiotherapy (RT) or systemic therapy (ST) remains controversial, especially in non-ocular cases. RT may be considered for patients who decline surgery. Prognosis is influenced by multiple factors, including tumor location, size, clinical stage, and treatment approach.

This systematic review aims to compile & analyze demographic data, clinical features, histopathological patterns, differential diagnoses, treatment strategies and outcomes of intraoral sebaceous carcinoma cases reported in the English-language literature. Additionally, it seeks to improve enhance understanding of this rare lesion by its clinical presentation, histological variability, and prognostic implications.

**AIMS AND OBJECTIVES –**

Aim -To conduct a systematic review to assess the clinical and pathological characteristics of oral sebaceous carcinoma

Objectives - To know demographics, Clinical and histopathological features, differential diagnosis, treatment and patient outcomes in oral sebaceous carcinoma.

**MATERIALS AND METHOD**

The study protocol was registered on PROSPERO database. The PROSPERO registration number for protocol for this study is CRD42025639648.

Case reports and case series of Oral sebaceous carcinoma were retrieved by a systematic search of scientific databases, PubMed Central (National Library of Medicine), Google Scholar (Google, Mountain View, USA) and SCIENCEDIRECT with the keywords Sebaceous Carcinoma OR ‘Oral Cavity’ AND ‘oral mucosa’. Retrieved literature was scanned to identify any cases reported with a name differing from Case reports before the year 2000 were not included for the present review. An independent researcher searched the databases and identified 68 relevant studies.

Reference checks of the cases identified were also made to help snowballing or networking of the cases. A table was tabulated regarding author, year of publication, demographic data as age, gender, clinical features, histopathological features, and differential diagnosis treatment opted for each of the case reports included.

**SEARCH STRATEGY**

To find pertinent studies on the demographic, clinical and histological conditions and outcomes of sebaceous carcinoma , a thorough search was undertaken in the Google scholar, PubMed, sciencedirect and DOAJ database. The filters were fixed at article type (prospective, retrospective, cross-sectional studies), publication date (January 2003 till January 2023), and the best match option. Controlled vocabulary (MeSH terms in PubMed) and free-text terms in the titles and/or abstracts were used to define the search strategy in the database. The search strategies developed using Boolean operators for PubMed and databases is given below and the “screening process of studies is presented in the form of PRISMA flow-chart (Figure1).

**Keywords used were “**Patients with “Oral carcinoma” or Oral Sebaceous Carcinoma (P)” or “Sebaceous Carcinoma of oral cavity” or “Oral involvement of sebaceous carcinoma” or “Patient outcome in Oral sebaceous carcinoma” or patients with Oral Sebaceous Carcinoma OR sebaceous gland carcinoma OR sebaceous gland adenocarcinoma) AND (Oral cavity OR oral involvement OR oral region) AND (clinico-pathological features OR histopathological features OR IHC) AND (outcome OR prognosis)

**ELIGIBILITY CRITERIA**

**Inclusion Criteria**

Following articles are included

1.Case reports and case series on patients with intraoral sebaseous carcinoma from 2000-2024

2. Articles published in English

3. Case reports and case series, Case reports and case series with review between 2000-2024

**Exclusion Criteria**

Following articles are excluded:

1. Case reports and case series on patients with extraoral sebaseous carcinoma ,sebaseous carcinoma of major salivary glands

2. Articles published in other language

4. Abstracts

5. Randomized and nonrandomized clinical trials

6. All studies

7. Unpublished data.

8. Articles with incomplete data.

The references of the selected articles were also analyzed for additional studies.

The research question was set in accordance with the PICOT format.

**STUDY SELECTION:**

The study selection was done in three steps. All the titles were reviewed and based on the inclusion and exclusion criteria; appropriate studies were selected. For all the selected titles, abstracts were obtained and reviewed, from which appropriate abstracts were selected based on the criteria. Full-text articles were obtained and analyzed, and the final set was obtained keeping in mind the selection criteria.The initial search strategy yielded 690 references. After removing duplications and nonrelevant articles, the number of references reduced to 123. This number was further reduced to 13 based on abstracts and titles.

Fig .1 : PRISMA flow-chart

“Additional records identified through other sources (Google Scholar)”
**(n =1204)**

“Records identified through database searching (PubMed)**”**
**(n = 690)**

## Identification

## Identification

“Total Titles screened”
**(n =1894)**

“Records excluded after review of titles
**(n =1482)”**

“Titles screened for duplicate removal”

**(n= 412)**

##  Screening

Excluded- duplicates
**(n =289)**

“Abstracts screened”

**(n=123)**

“Records excluded (n=98) after review of abstracts”
**(n =776)**

##  Eligibility

“Full texts screened on basis of inclusion and exclusion criteria”

**(n=25)**

“Studies excluded after review of full text **(n=12)”**

##  Included

“Studies included in qualitative synthesis (n=13)

**13 estimates”**

**ASSESSMENT OF RISK OF BIAS**

Risk of bias assessment of all the included studies was performed. All the included studies were case reports; about 2 studies included 2 cases. For the risk of bias assessment of included case reports, JBI critical appraisal checklist for Case reports was used to assess Risk of bias of included case reports. t has been found that most of the case reports included showed all of the items of appraisal with a “yes” response across all the studies. Thus, when the overall quality assessment or Risk of bias is done; it can be interpreted that all of the included case reports showed better quality of assessment.

**RESULTS**

The search strategy retrieved 1894 articles. 1482 records excluded after review of titles 412 titiles remaining screened for duplication out of which 289 excluded. Assessment of the full text was done for 123 articles after which 13 were included in the study. All included paper were published between 2000 to 2024.

The present systematic review was conducted to assess demographics, Clinical and histopathological features, differential diagnosis, treatment and patient outcomes in oral sebaceous carcinoma. The screening process was undertaken in three steps that included screening of titles followed by screening of abstracts and finally screening of full text for inclusion in the review. The characteristics of the studies included in the systematic review are presented in the below tables.”

The table 1 represents study characteristics with respect to age group, patients, exposure and primary and secondary outcomes with follow-up of the included studies. The age of the study participants across the studies varied from 40 years to 81 years; with mean age around 60 years. All the cases involved in the studies were having sebaceous carcinoma of the oral region. In majority of the studies the region affected was upper or lower lip, followed by tongue and palate. Clinically on extra oral examination the lesion appeared as markedly ulcerated, exophytic, irregularly shaped, indurated mass varying in dimensions. The most common diagnosis arrived at was Sebaceous carcinoma of the oral region. The common histo-pathological findings across the included studies were presence of neoplastic cells which showed a range of sebaceous differentiation with finely vacuolated rather than clear cytoplasm. Immunohistochemistry showed strong nuclear immunoreactivity with Androgen Receptor and scattered membranous and cytoplasmic reactivity with EMA and positive for S-100 protein, EMA, but negative for CEA. The differential diagnosis was squamous cell carcinoma, basal cell carcinoma and malignant salivary gland neoplasm.The treatment fiven for most of the cases was incisional biopsy followed by wide local excision of the residual tumour; followed by chemotherapy and radiotherapy if required. Amongst all the cases reported in this systematic review, about 2 cases showed lymph node involvement with distant metastases.

**Table 1- Details of the study participants, intervention, and comparator of the studies included in the systematic review**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| SR NO | Authors name  | No of reported cases | Demographic data  | exposure | Histopathological features | Differential diagnosis | treatment | Patient outcome |
|  |  |  | Age /Sex | site | Appearance  | Size & features | Duration | TNM staging |  |  |  |  |  |  |
|  | Handschel J et al 2003 | 1 | 80/F | Edentulous alveolar ridge of the mandible | ulcerated | 1.5 × 1.2 cm lesion in the anterior floor of the mouth | 6 months | NR | Intraoral sebaceous carcinoma | solid cords and nests, the centralportions of which were often filled with clear cells showing a honeycombed cytoplasm | CEA showed specifically stained tumourcells with foamy cytoplasm | NR | excised with a 1-cm margin of healthy tissue including Sebaceous carcinoma in the anterior floor of the mouth. | postoperative coursewas uneventful. |
|  | Alawi F et al 2005 | 1 | 66/M | upper lip. | bleeding sore’’ | markedlyulcerated, exophytic, irregularly shaped, indurated mass of the upper left labial mucosa, measuring 1.5 X 3 X 1.0 cm in size | 3 years | NR | Sebaceous carcinoma of the oral mucosa | severely dysplastic squamous epithelium exhibiting transitionto an infiltrating malignant neoplasm composed of islands andsheets of anastomosing basaloid epithelial cells with areas ofprominent sebaceous differentiation. | strong nuclear immunoreactivity with AR andscattered membranous and cytoplasmic reactivity with EMA, completely unreactive withthe AR antibody. | squamous cell carcinoma and malignant salivary gland neoplasm. | incisionalbiopsy was performed and wide localexcision of the residual tumor | After 1 year of follow-up, therehas been no evidence of local recurrence or metastasis. |
|  | Gomes CC et al 2007 | 1 | 55/M | continuouspain and severe trismus in the posterior mandible  | right side of the mandible | swelling in theangle of the right side of the mandible could beobserved, as well as submandibular and anterior cervicallymph nodes enlargement. | 3 months | NR | Intraoral sebaceous carcinoma | surfacemucosa with inWltrating nests and sheets of eosinophilicepithelial cells exhibiting prominent nucleoli,moderate cellular and nuclear polymorphisms andpoorly deWned cellular outlines. centrally located vesicular-shaped nuclei and exhibitingvacuolated or foamy cytoplasm | androgen receptor (CloneAR441, Dako, Carpinteria, USA) revealed positivenuclear staining  | squamous cell carcinoma, basal cell carcinoma | incisional biopsy, chemotherapy inassociation with radiotherapy | Follow-up done |
|  | Oshiro H et al 2010 | 1 | 66/M | Mass like  | tongue | tumorous lesion located in the dorsal andmidline part of the tongue, measuring about 25 mm in greatestdiameter  | 1 month | T2N2cM0primary lingual tumor. | Primary sebaceous carcinoma of the tongue | neoplastic sebocytic and basaloidcells, and Sudan III staining and electron microscopyrevealed intracytoplasmic lipid droplets. | neoplastic cellsstained positive for adipophilin; epithelial membraneantigen; epithelial antigen; and cytokeratins 7, 8, and 15, butnegative for cytokeratins 5/6, 18, 19, and 20; the androgenreceptor; and carcinoembryonic antigen | basal cell carcinoma and squamous cell carcinoma | Superselectiveintraarterial chemotherapy and neck dissection | patient died 17months after completing the initial course of chemoradiotherapy. |
|  | Wang H et al 2010 | 1 | 50/M  | Mass like growth and pain | Buccal mucosa  | 4.8 X4.6 X2.7 cm broadbased,fungating, and friable mass on the left posterior buccalmucosa extending to the retromolar trigone and abutting onthe left mandibular body without invasion of the bone. | 3 months | NR | Sebaceous carcinoma of the oral cavity: | sebaceous nests (70%),squamous islands with keratin pearl formation (2%), andpoorly differentiated solid areas (28%). | neoplastic cells displayed characteristic membranous and cytoplasmicstaining for epithelial membrane antigen (EMA).The basaloid and sebaceous cells demonstrated strong nuclearimmunoreactivity to androgen receptor | Squamous cell carcinoma | tumor was completely resected. All neck lymph nodes werenegative for carcinoma. The patient received radiation therapyafter the surgery | 5-yearsurvival with sebaceous carcinoma in the salivaryglands is 60% |
|  | Wetzel S et al 2014 | 1 | 75/M  | erythematous raised ulcerated lesion | attached maxillary gingiva buccally | NR | NR | NR | Sebaceous carcinoma of the maxillary gingiva | stratified squamousepithelium showing transition to a malignant tumor comprised of lobules of epithelialcells exhibiting sebaceous differentiation | lesional cells reacted with androgenreceptor (Figure 2A) and epithelial membrane antigen (EMA)  | squamous cell carcinoma and basal cell carcinoma | surgical excision. Adjuvant radiation therapy andchemotherapy may also be given | rare occurrence of intraoral SC overallsurvival rates have yet to be determined. |
|  | Greenall CJ and Drage NA 2015 | 1 | 81/M | Firm , irregular mass  | upper right lip | poorly defined ,hypoechoic irregular mass in the right naso-labial region, with no internal vascularity, involving skin, subcutaneous fat, orbicularis oris and the intraoral mucosa  | Since 2 month | NR | Sebaceous carcinoma of the lip | cells of salivary gland origin could be either reactionary or malignant. | NA | basal cell carcinoma,and malignant tumours | palliativeradiotherapy | Ultrasound may be useful in aiding the early surgical planning for patients with extensive dermatologicaldisease. |
|  | Rowe M et al 2015 | 1 | 76/M | exophytic lesion | upper gum with associated mobility of the adjacent teeth | gingival tumor was1.5 X 1.4 X 1.1 cm and invaded the underlying bone | 6 weeks | NR | Intraoral sebaceous carcinoma metastatic to the lung and subcutis | neoplastic proliferation was composedof epithelioid cells with round to oval nuclei, small toprominent nucleoli, and clear to vacuolated appearingcytoplasm | PMS-2, MLH-1, MSH-2, and MSH-6 showed nuclear reactivi | NR | partial maxillectomy | no previous case has an intraoralsebaceous carcinoma metastasized to another dermalregion of the body |
|  | Jawanda MJ et al 2018 | 1 | 40/F | Swelling  | Right side invoving buccal mucosa  | swelling was firm in consistency, nontender, and of approximately5 × 4 cm, extending superoinferiorly from the infraorbitalridge to 2cm above the inferior border of the mandibleand anteroposteriorly from the right corner of the mouth to1.5cm anterior to the tragus | 1 year | NR | Intraoral Sebaceous Carcinoma | large nests of neoplasticcells with squamous appearance, separated by scantystroma (Figure 2). The neoplastic cells had large vesicularnuclei with prominent nucleoli. Cellular and nuclear pleomorphismwith few nuclei showing multilobation was seen,along with typical and atypical mitotic figures | Not performed | metastaticclear cell renal carcinoma | complete excision verified by negative margins.Radiotherapy is used if metastatic disease and/or a high riskof recurrence are present. Multiagent chemotherapy hasbeen used to treat recurrent disease | NR |
|  | Ambrosino M et al 2021 | 1 | 71/M | Ulcerated  | Lower lip | markedly ulcerated, exophytic, irregularly shaped, indurated mass of the lowerright labial region, measuring 1.8 cm in size | 1 year | NR | Sebaceous Carcinoma of The Lip | Neoplastic cells showed a range of sebaceous differentiation with finely vacuolated rather than clear cytoplasm | Neoplastic cells werepositive for S-100 protein, EMA, but negative for CEA | squamous cell carcinoma, basal cell carcinoma with sebaceousdifferentiation and salivary gland neoplasm | Surgery | patient underwent a complete clinical and radiographic evaluation to identify any regional or distant metastases |
|  | Lu Q et al 2021 | 1 | 62/M | Growth like mass  | Palate  | a small nodule(0.5 cm × 0.5 cm) appeared beneath the mucosa; however,it gradually grew to its present size of 2.0 cm × 1.5 cm) | 1 year | NR | Sebaceous carcinoma of the right palate: | inconclusive patternbut strongly suggested that malignancy originated inthe salivary gland | PAS(–), EMA(+), AR (+) | squamous cell carcinoma (SCC) andmucoepidermoid carcinoma | Surgery, Postoperative chemotherapy and radiotherapy were notadopted in the present case, as | Patient was relatively satisfiedwith the surgery |
| 12 | Cosola MD et al 2022 | 1 | 71/M | Ulcerated  | Lower lip | markedly ulcerated, exophytic, irregularly shaped, indurated mass of the lower rightlabial region, measuring 1.8 cm in size. | 1 year | NR | Sebaceous carcinoma of the lip: | nodulesor sheet of cells separated by a fibrovascular stroma. The neoplastic tissue was deeply infiltrating, involving thesubmucosa and even the underlying muscle. | Neoplastic cells were positive for S-100 protein and epithelial membraneantigen, but negative for carcinoembryonic antigen | squamous cell carcinoma, basal cell carcinoma with sebaceous differentiation, and salivary gland neoplasms | excisional biopsy with 0.5 cm of free margins and W-shaped wedge was performed; | patient underwent a complete clinical and radiographic evaluation to identify any regional or distant metastases. |
| 13 | Katib Y et al 2024 | 1 | 47/M  | Ulcerated , painless mass  | Upper lip | ulcerated, exophytic, andirregularly shaped mass was observed on the upper lip  | 1 year | Lymph node showed no metastases  | oralsebaceous carcinoma in theupper lip | malignanttumor with a nodular pattern consisting of basaloid cells with obvioussebaceous differentiations and frequent mitoses | neoplastic cells testedpositive for broad-spectrum cytokeratin (AE1-AE3), epithelial membraneantigen (EMA), and P53, while testing negative for S-100 andcarcinoembryonic antigen (CEA). | basal cellcarcinoma (BCC), squamous cell carcinoma (SCC), and asalivary gland tumor. | lip-wide localexcision with reconstruction using a local flap and leftmodifiedradical neck dissection. | Three months post-RT, magnetic resonanceimaging (MRI) scan indicated no tumor recurrence |

NR –Not reported, NA- Not Available

 **Discussion –**

Sebaceous carcinoma (SC) is a rare epithelial neoplasm that typically originates in the ocular adnexa, most commonly from the meibomian glands or the glands of Zeis21. By definition, SC is a cytologically and/or architecturally malignant tumor characterized by exclusive sebocyte differentiation22. Although sebaceous glands are found in various anatomical sites, the majority of sebaceous tumors, including SC, arise in the head and neck region. Although Sebaceous Carcinoma demonstrate a marked predilection for the ocular area—particularly the upper eyelids—approximately 25% of cases develop in extraorbital locations, with the parotid gland accounting for nearly 30% of these extraorbital cases23.

Glands exhibiting Sebaceous differentiation are frequently identified in glands within the oral cavity, and similar differentiation may also be observed in the major salivary glands24. Sebaceous glands are found in an approximately 10%–40% of normal parotid glands and 6%–10% of submandibular glands25. Despite this presence, both benign and malignant sebaceous tumors of the salivary glands remain extremely rare, constituting less than 0.2% of all major salivary gland neoplasms25. In contrast, Fordyce granules—ectopic sebaceous glands—are commonly seen in the oral mucosa of up to 80% of adults26.

Clinically, Fordyce granules appear as grossly as rice-like, asymptomatic, white or yellow papules ranging from 1–3 mm in diameter27. Histologically, they are composed of approximately 15 well-differentiated sebaceous lobules per gland. Although their precise function remains unclear, they have been associated with hyperplasia (15 well-differentiated lobules per gland), adenoma (sharply demarcated mass lesion), or carcinoma (demonstrating cytologic atypia and infiltrative growth)3,28 The first case of intraoral sebaceous carcinoma (SC) was reported by Damm et al. in 1991.

Among the 13 case reports analyzed in this study, 10 were male, suggesting a possible male predominance; however, previous literature doesn’t confirm a gender predilection. Intraoral Sebaceous Carcinoma typically occurs in adult with patient ages ranging from 40 to 81 years and an average age of approximately 60 years. These findings are consistent with the literature, where the average reported age is 60.2 years, as noted by Wetzel et al. (2014)28. While most cases occurred in individuals over 50, two notable cases reported by Jawanda et al. (2018)29 and Katib et al. (2024)10 involved a 40-year-old female and a 47-year-old male, respectively. Among the 13 reported cases, several patients had a positive history of smoking, alcohol use, or tobacco consumption. However, no definitive correlation between these habits and the development of sebaceous carcinoma has been established.

Clinically the lesion presented with variable features including ulceration , mass like growth , bleeding sore, exophytic growth. Cases reported by Cosola et al (2022)30 , Alawi et al(2005)25 , Qun lu et al (2021), Wang et al (2010), Wetzel et al (2014)28, Handschel et al(2003)24, Gomes et al (2007) described lesion as ulcerated, exophytic, irregularly shaped, indurated mass. Katib et al (2024)10 described lesion as nodular. Three cases reported by Oshiro et al (2010)31 , Greenall et al(2015) and Jawanda et al (2018) described lesion as swelling with intact mucosa. Jawanda et al (2018) noted the swelling as mobile with no ulceration of the overlying skin. Intraoral examination revealed no obvious swelling with intact oral mucosa. Oshiharo et al (2010) described a submucosal mass-forming lesion on the dorsal part of the tongue that was covered by a smooth mucosal layer & associated with redness .Greenall et al(2015)34 reported a lesion on the upper right philtrum as erythematous and indurated, the overlying skin remained intact.

Sebaceous glands of the oral cavity are known as Fordyce granules6. They are present in approximately 80% of adults. Primary sebaceous carcinoma of oral cavity is thought to originate from Fordyce granules or salivary gland elements6.  Among the 13 cases reviewed, only 2 cases reported by Jawanda et al( 2018)29 and Alawi et al (2005)25 confirmed the presence of fordyces granules. Alawi et al 2005 et al described them as numerous Fordyce granules measuring 1-2 mm in diameter primarily involving the upper labial mucosa. Fordyce granules were also noted bilaterally in the buccal mucosa and in the lower labial vestibule. In both the cases fordyces granules were present in the proximity of the lesion. The most common site of involvement was the upper and lower lip, followed by buccal mucosa , tongue, gingiva and floor of mouth.

Duration of lesion ranged from 6 weeks to one years. Only one case exhibited cervical lymphadenopathy. Oshiro et al (2010) reported whole-body CT finding of bilaterally enlarged cervical lymph nodes , suggesting regional lymph node metastasis. No distant metastases were observed. Based on these results, the lesion was classified as T2N2cM0 using the International Union Against Cancer guidelines.

Various radiographic modalities including CT Scan , MRI , CBCT, OPG have been used to asses soft and hard tissue. Gomes et al (2007) reported CT , OPG findings as Bone loss and invasion of underlying submucosa and muscles. Grennell et al (2018) described the Ultrasonographic features of lesion as a poorly defined hypoechoic irregular mass in the right naso-labial region, with no internal vascularity. The lesion involved the skin, subcutaneous fat, orbicularis oris and the intraoral mucosa. In case reported by of Jawanda et al 2018 , Water’s view of the skull revealed a soft tissue swelling in the right cheek area. Oshiro et al (2010) , confirmed a tumorous lesion on CT and MRI revealed located in the dorsal and midline part of the tongue, measuring approximately 25 mm in greatest diameter. Fluorine-18-fl uorodeoxyglucose positron emission tomography (FDG-PET) showed an area of high uptake, with a maximum standard uptake value of 7.0, corresponding to the lingual lesion.

Ultrasound guided fine needle aspiration cytolopathology reported by Grennell et al 2018 suggested the lesion originating from salivary gland which could be either reactionary or malignant. Qun Lu et al (2021) found no significant findings.

Histologically, sebaceous neoplasms of the salivary glands are divided into 5 categories: sebaceous adenoma, sebaceous lymphadenoma, SC, sebaceous lymph adenocarcinoma, and sebaceous differentiation in other tumors35. Microscopically, the tumor mass appeared to be situated in the deeper mucosa with pushing margins of tumor nests35. The tumor was consisted of large nests of neoplastic cells with squamous like features , separated by scanty stroma The cells exhibited large vesicular nuclei with prominent nucleoli. Cellular and nuclear pleomorphism with few nuclei showing multilobation , along with typical and atypical mitotic figures. The sebaceous nests were composed of clear tumor cells with foamy cytoplasm. Handschel et al 2003 described similar tumour arranged in solid cords and nests, with the central portions often filled with clear cells showing a honeycombed cytoplasm . Additionally ashiro et al (2010) decribed lesion with enlarged nucleoli and bubbly cytoplasmic vacuolization. These cells had a moderate to high nuclear to cytoplasmic ratio and moderate to high degree of nuclear pleomorphisms. More than 10 mitotic figures per 10 high-power fields were observed. Pyknosis, karyorrhexis, and individual cell death were observed, and the cells formed irregularly lobulated solid nests. Comedo-type necrosis was absent. Nuclear palisading was evident at the periphery of the nests, but no keratinization or intercellular bridging was observed. Alawi et al (2005) also reported areas of marked squamous differentiation and keratin pearl formation. Area of necrosis was also evident. Electron microscopy by Oshiro et al (2010) revealed that the neoplastic cells contained small intracytoplasmic lipid droplets ranging in size from 800 to 1,200 nm in diameter.

According to Plaza et al.16, histopathology remains the gold standard for the diagnosis of SC. They suggested that the immunohistochemical assessment of epithelial markers and lipid droplet-associated proteins serve as a valuable diagnostic adjunct. Numerous studies have shown that the neoplastic cells stain positive for various epithelial markers, including cytokeratins, EMA, and c-erbB2 (Her-2/neu)34-37 Carcino Embryogenic Antigen was expressed in stained tumour cells with foamy cytoplasm. In contrast, gross cystic Q2markers are typically negative29 SC also demonstrate diffuse nuclear staining for Androgen Receptor. Carolina *et al.* viewed Androgen Receptor as a better marker of sebaceous differentiation than EMA. c-erbB2 showed a cytoplasmic weak membranous and cytoplasmic staining in most tumour cells.

Neoplastic cells also shows exhibits diffuse positivity for broad spectrum cytokeratin (AE1/AE3); focally positive for cytokeratin 7, cytokeratin 8, low molecular weight keratin (CAM 5.2), and cytokeratins 15 and 19; but negative for cytokeratins 5/6, 18, and 20. The neoplastic cells are negative for carcinoembryonic antigen. Increased expression of protein P53 and high proliferative index expressed by Ki67 estimated about 50% in hotspot areas. Positivity for Both EMA and AR, confirms the vacuolated clear cells are not mucus cells or squamous cells containing rich in glycogen. Based on these findings, Squamous Cell Carcinoma, clear cell melanoma, and Basal cell Carcinoma can be ruled out.

Due to the infiltrative growth pattern, necrosis, and cytologic features of Sebaceous Carcinoma, malignant neoplasms may be considered in diffrential diagnosis. However, the histologic appearance of SC is often characteristic. Basal cell carcinomas exhibiting sebaceous differentiation, clear cell variants of basal cell, and squamous cell carcinoma and eccrine carcinomas, balloon cell melanomas, and metastatic clear cell tumors, may be confused for cutaneous SC. Jawanda et al highlight differential diagnosis of intraoral SC which includes clear cell as well as basaloid squamous cell carcinoma with hydrophilic swelling, metastatic clear cell renal carcinoma, and salivary gland malignancies including mucoepidermoid carcinoma, solid-type adenoid cystic carcinoma, basal cell adenocarcinoma, and salivary duct carcinoma. Notably basal cell carcinoma is characterized by superfcial plate-like proliferation of basaloid and/or squamoid cells, that broadly to the overlying epidermis.

Mucicarmine and PAS stain can helps to rule out Mucoepidermoid carcinoma and Sqamous cell carcinoma with hydropic degeneration. Sudan IV & Oil Red O are Sudan IV are useful for diagnosis of sebaceous cells. The cytoplasm of these cells stained negative with mucicarmine and periodic acid Schiff (PAS) stains, with/without diastase, confirming that the vacuolated clear cells were neither mucus nor glycogen-rich squamous cells.

The pathogenesis of intraoral SC is mysterious and requires further elucidation. The pathogenesis of sporadic SC remains unclear. According to Alawi et al (2005) , A report has demonstrated loss of either hMLH-1 or hMSH-2 in 3 of 14 sporadic SC tumors. But these results are in contrast with other studies have reported. Thus, additional studies are necessary in order to determine whether loss of these or other mismatch-repair genes are responsible for the development of sporadic SC

Only one case reported by Rowe et al 2015 showed distance metastasis. In that case a nodule & multiple hypermetabolic lymph nodes in the right lower anterior mediastinum as well as nodules scattered throughout the bilateral lung fields, cutaneous-based nodule was observed in the upper inner left thigh & a smaller focus was seen in the left buttock. Because of the multiple sebaceous carcinoma suspicion ,additional IHC panel for PMS-2, MLH-1, MSH- 2, and MSH-6 n was conducted. Result showed nuclear reactivity, indicating that there was no immunohistochemical evidence of microsatellite instability as might be expected in sebaceous tumors seen in Muir–Torre syndrome. Thus the possibility of Muir–Torre syndrome was rule out.

The treatment of choice for sebaceous carcinoma is surgery, with complete excision verified by negative margins. Radiotherapy is used if metastatic disease and/or a high risk of recurrence is present. Multiagent chemotherapy has alsobeen used to treat recurrent disease . Nevertheless, an increased proclivity for local recurrence and metastasis calls for a long-term follow-up of the affected patients.

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