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# Lung cancer metastasis to oral soft tissues: Systematic review of 122 cases

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## Abstract

Background: Lung cancer metastasis to oral region is very rare. Studies have been published analysing the cases of metastatic tumours to the oral cavity by many researchers. But very few research work has been conducted till date to analyse the lung cancer metastasis as the soul primary source particularly to the oral soft tissues. The goal of this study was to examine the published cases of oral soft tissue metastasis from lung cancer as the only primary source from 1st August 1977 to 31st December 2021.

Materials and methods: An electronic search of the published English literature was performed in PubMed/ Medline, Scopus, Google Scholar, and Research gate databases, using keywords like 'Lung cancer', OR/ AND 'Lung carcinoma' OR/ AND 'Oral cavity', OR/AND 'Metastasis', OR/AND 'Primary', OR/AND 'Source', OR/AND 'Initial', OR/AND 'Tongue', OR/AND 'Palate', OR/ AND 'Tonsil', OR/AND 'Lip', OR/AND 'Buccal mucosa', OR/AND 'Floor of mouth', OR/AND 'Salivary glands', OR/ AND 'Parotid', OR/ AND 'Submandibular', OR/ AND 'Sublingual' OR/ AND 'Mandible', OR/AND 'Maxilla. We also searched all related journals manually. Reference list of all articles was also checked.

Results: Our research revealed total 122 patients. The most prevalent diagnosed metastatic lung cancer was adenocarcinoma. Gingiva, tongue and tonsils were the most common site of metastasis. 54% patients died of metastasis with a survival time of 1 week to 2.5 years.

Conclusions: Oral soft tissue metastasis from lung cancer has a bad prognosis. More cases need to be published in order to raise awareness of these lesions and gain a better understanding of their characteristics.

***Key words:*** *Lung cancer, metastasis, oral, primary, soft tissues.*

## Introduction

GLOBOCAN databases has documented lung cancer (LC) as the 2nd most common diagnosed cancer leading to high mortality after breast cancer worldwide (1). The unique feature of LC is its long term asymptomatic clinical presentation and when the disease reaches in its advanced stages, it is associated with a high risk of developing distant metastasis. It has been found that most of the time, the symptoms are disregarded by the patients even once they arise, resulting in a delay in diagnosis and treatment (2). The most common regions of distant metastasis via LC in the body are liver, kidney, adrenals, brain, bones, scalp, and other organs (3). Oral cavity is the uncommon site of LC metastasis, and mostly affects soft tissues rather than jaw bones (JB) (4). The prognosis for such cases is poor, indicating the critical importance of their early identification and management. Due to their strong resemblance to some benign growths, late appearance, or lack of interpretation, diagnosis of these metastatic lesions remains difficult for clinicians and pathologists (5). Studies have been published analysing the cases of metastatic tumours to the oral cavity by many researchers. But very few research work has been conducted till date to analyse the lung cancer metastasis as the soul primary source particularly to the oral soft tissues (OST). The goal of this research was to examine published cases of oral soft tissue metastasis (OSTM) from LC as the sole primary source in the literature from 1st August 1977 to 31st December 2021, and to learn about their characteristics.

## Material and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards were used to conduct this research. There was no need to seek any ethical approval because of the nature of the current review.

- Focused PECO question

For conducting this review, we framed a focused PECO question 'How many cases of OSTM from LC as the sole primary source have been documented in the literature and what is the prognosis of these metastatic lesions'?

Population: Patients with OSTM from LC

Exposure: Distant metastasis of LC

Comparator: Not applicable for current research

Outcome: Prognosis of OSTM from LC

- Search strategy for identification of studies (Fig. 1)

An electronic search of the published English literature was performed in PubMed/ Medline, Scopus, Google Scholar, and Research gate databases, using keywords like 'Lung cancer', OR/ AND 'Lung carcinoma' OR/ AND 'Oral cavity', OR/AND 'Metastasis', OR/AND 'Primary', OR/AND 'Source', OR/AND 'Initial', OR/ AND 'Tongue', OR/AND 'Palate', OR/ AND 'Tonsil', OR/AND 'Lip', OR/AND 'Buccal mucosa', OR/AND 'Floor of mouth', OR/AND 'Salivary glands', OR/ AND, Mandible', OR/AND 'Maxilla'. We also searched all related journals manually. Reference list of all articles was also checked.

- Screening of studies

The current review involved three steps screening of

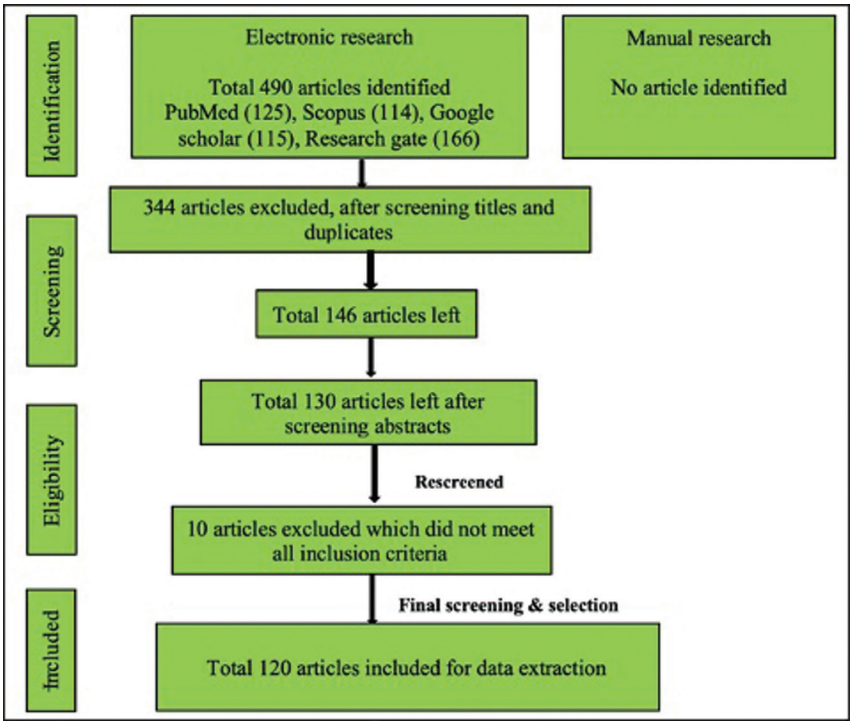


**Fig. 1**: PRISMA flowchart showing search strategy.

the studies. In the first step, titles were reviewed by two authors (SG, MKJ) independently and duplicates were removed. Then four authors ( NBK, ARD, AG, KS) reviewed the selected abstracts of all the reports independently. In the final stage, the text of selected studies was screened by authors separately (SKY, ABY). Full report was collected, discussed, and resolved for cases among all authors that appeared to fit the inclusion criteria or for which evidence was insufficient to make a clear determination.

- Inclusion criteria

• Confirmed cases of OSTM from LC as the sole primary source. Papers included were from 1st August 1977 to 31st December 2021.

• Type of studies: Case reports, letter to editor, Short communication, Retrospective analysis and correspondence.

• Cases were selected beyond the restriction of limitations on parameters such as age, gender, ethnicity or socioeconomic status, etc.

• Articles published only in English language were included.

- Exclusion criteria

• Cases with no definite diagnosis of OSTM from LC as the sole primary source.

• Publications reporting the OSTM from any other site than lung.

• Cases of Jaw bone metastasis from LC as the primary source.

• Other epidemiological studies, cross-sectional studies and cohort studies were excluded as they did not provide individual patient's data.

• Review articles, editorials, conference abstracts, hypothesis papers, web news, media reports, animal studies.

- Outcome measures

1. Primary outcome measures: To evaluate the number of cases of OSTM from LC as the sole primary source reported in the literature and to determine their prognosis.

2. Secondary outcome measures: To evaluate factors such as: World-wide distribution of cases of OSTM from LC, Patient's demographic details, Associated risk factors, Predominant site of OSTM from LC, Clinical features of these metastatic lesions, Most prevalent type of metastatic LC and Type of therapies used to treat such metastatic lesions.

- Risk of bias assessment

Most of the studies included in this review were case reports. Risk of bias in the included studies were appraised following CARE checklist guidelines. In many of the studies, there was missing information regarding many parameters used for data extraction in our research. We tried reaching the authors of those cases to clarify this bias; however we were unable to recover the missing information.

- Data extraction & analysis

After study selection, screening and a thorough examination, the data were extracted. The information gathered was cross-checked and tabulated into three tables (Table 1-3 cont.-2). In case of missing data, 6 weeks' time was given to gather the information. If the information was still missing, we then indicated the missing data as "Not available (NA)" in the text and in the tables.

## Results (Table 4, 4 cont.-1)

Results were expressed in descriptive statistics. There were 111 Case reports, 3 Letter to editor, 3 Short communications, 2 Correspondences, and 1 Retrospective analysis. There were 122 patients in total, with 100 males (82%) and 22 females (18%). The maximum number of cases were from Japan (n-31), India (n-14), and USA (n-13). The patients' average age was 60.8 years (range 25-87). Mean age was 61.4 years in males and 58.3 years in Females. 35 of the 122 patients (28.7%) had a previous history of LC, while the other 78 had none (63.9%) . 54.1% had associated risk factors or underlying comorbidities. Most OSTM metastasis was found in Gingiva (41.8%)>tongue = tonsils (17.2%)>parotid glands (11.5%)>submandibular glands (4.1%))> palate (2.5%)>lip (1.6%)>retromolar trigone = buccal mucosa (0.8%). Patients presented with variable clinical features. OST were the initial site of metastasis in 60.6% individuals. OST were the only site of metastasis in 51.6% of cases, whereas 44.2% cases involved other parts of the body also. The most common type of LC diagnosed was Adenocarcinoma (n-46). The most common treatment aids included combined Radiotherapy and chemotherapy (25.4%), followed by chemotherapy alone (22.1%). 66 individuals (54.1%) died with a mean survival rate of 1 week to 2.5 years.

## Discussion

Metastasis to the oral cavity is a rare occurrence, with the real incidence unclear (1-2% of all oral cancers). Because of their rarity, they are sometimes overlooked for a long time before being discovered and are diagnosed during investigations. According to epidemiological investigations, LC is the most common primary source of OSTM, while Breast cancer is the most common source of JBM (5). In this study, we found 122 documented cases of OSTM from LC as the sole primary source.

Studies reveal that OSTM affects both genders equally with peak incidence of 5th- 6th decade with a male majority (5). In the current study also, there was a male predominance, with M: F = 4.5:1 with age from 2nd-8th decade. According to studies, Smoking and tobacco consumption habits are strongly linked to the development of LC. Nicotine and its derivatives, which are found in tobacco and smoke, help to promote the expression of oncogenic proteins which leads to the spread of cancer

**Table 1**: Demographic data of patients with oral soft tissue metastasis from lung cancer as the sole primary source (1st August 1977 to 31st December 2021).

| S.NO. | Authors/ Year | Country | Age of patient (years) | Gender | Previous history of lung cancer | Associated risk factors/ Medical history/ comorbidities |
|---|---|---|---|---|---|---|
| 1. | Ellis *et al*. 1977 | USA | 58 | M | N | N |
| 2. | Kim *et al*. 1979 | Japan | 74 | M | N | S |
| 3. | Brodasky *et al*. 1984 | USA | 45 | M | N | NA |
| 4. | Monforte *et al*. 1987 | Spain | 25 | M | N | N |
| 5. | Shalowitz *et al*. 1988 | USA | 54 | M | N | S |
| 6. | Seddon *et al*. 1989 | UK | 83 | F | N | S |
| 7. | Sehab *et al*. 1994 | UK | 70 | M | Y | S |
| 8. | Alandez *et al*. 1995 | Spain | 47 | M | Y | S |
| 9. | Hisa *et al*. 1998 | Japan | 61 | M | N | N |
| 10. | Takatsugi *et al*. 1998 | Japan | 48 | F | N | N |
| 11. | Kadokura *et al*. 1999 | Japan | 54 | M | N | N |
| 12. | Piatettli *et al*. 1999 | Italy | 52 | M | N | N |
| 13. | Murakawa *et al*. 2001 | Japan | 52 | F | Y | NA |
| 14. | Viera *et al*. 2001 | Brazil | 57 | M | NA | S |
| 15. | Garcia-Raja *et al*. 2002 | Spain | 63 | M | Y | S, IHD |
| 16. | Seigo *et al*. 2002 | Japan | 51 | F | N | N |
| 17. | Tanaka *et al*. 2002 | Japan | 64 | M | NA | NA |
| 18. | Tanaka *et al*. 2002 | Japan | 64 | M | NA | NA |
| 19. | Tanaka *et al*. 2002 | Japan | 68 | M | NA | NA |
| 20. | Yoschii *et al*. 2002 | Japan | 61 | M | NA | N |
| 21. | Aoe *et al*. 2002 | Japan | 84 | M | N | S |
| 22. | Cassarino *et al*. 2003 | USA | 64 | M | Y | S |
| 23. | Zanconatti *et al*. 2003 | Italy | 71 | M | Y | N |
| 24. | Borg *et al*. 2004 | Australia | 54 | M | N | N |
| 25. | Soyuer *et al*. 2004 | Japan | 50 | F | N | FHOLC |
| 26. | Terashima *et al*. 2004 | Japan | 63 | M | N | S |
| 27. | Boeger *et al*. 2005 | Germany | 54 | M | N | N |
| 28. | Huang *et al*. 2005 | Taiwan | 49 | M | N | S |
| 29. | Ischibashi *et al*. 2005 | Japan | 71 | M | NA | N |
| 30. | Tho *et al*. 2005 | UK | 70 | M | NA | N |
| 31. | Tsubochi *et al*. 2005 | Japan | 39 | M | Y | S |
| 32. | Glazar *et al*. 2006 | USA | 69 | M | Y | S, A, As. |
| 33. | Jagur *et al*. 2006 | Brazil | 52 | M | N | NA |
| 34. | Kurt *et al*. 2006 | Turkey | 57 | M | N | S |
| 35. | Park *et al*. 2006 | South Korea | 55 | M | N | NA |
| 36. | Curein *et al*. 2007 | France | 64 | M | Y | NA |
| 37. | Hantiti *et al*. 2007 | Tunisia | 47 | M | N | NA |
| 38. | Higginson *et al*. 2007 | USA | 68 | M | Y | NA |
| 39. | Mastronikolis *et al*. 2007 | Greece | 71 | M | Y | S, A, HT, CD, CC, PH. |
| 40. | Callifano *et al*. 2008 | Italy | 60 | M | N | N |
| 41. | Hatoum *et al*. 2008 | Beirut | 63 | F | N | S |
| 42. | Pozzi *et al*. 2008 | Switzerland | 57 | F | NA | N |
| 43. | Watanabe *et al*. 2008 | Japan | 66 | F | N | NA |
| 44. | Hashitani *et al*. 2009 | Japan | 59 | F | N | As. |

**Table 1 cont.**: Demographic data of patients with oral soft tissue metastasis from lung cancer as the sole primary source (1st August 1977 to 31st December 2021).

| | | | | | | |
|---|---|---|---|---|---|---|
| 45. | Sugiura *et al*. 2009 | Japan | 66 | F | N | HT |
| 46. | Yaren *et al*. 2009 | Turkey | 63 | M | Y | S |
| 47. | Wu *et al*. 2009 | China | 36 | F | Y | N |
| 48. | Gupta *et al*. 2010 | India | 68 | M | N | S, DM, HT. |
| 49. | Guven *et al*. 2010 | Turkey | 60 | M | Y | MI, S |
| 50. | Kirke *et al*. 2010 | Australia | 71 | M | Y | S, As. |
| 51. | Mavilli *et al*. 2010 | Turkey | 58 | F | N | N |
| 52. | Moharil *et al*. 2010 | India | 40 | M | N | S, A |
| 53. | Ulubas *et al*. 2010 | Israel | 59 | M | N | N |
| 54. | Beena *et al*. 2011 | India | 49 | M | N | N |
| 55. | Dhawad *et al*. 2011 | India | 46 | M | NA | A, Ascites, Hernia |
| 56. | Lopez- Jornet *et al*. 2011 | Spain | 76 | M | N | S |
| 57. | Moser *et al*. 2011 | Switzerland | 75 | M | Y | As |
| 58. | Murey *et al*. 2011 | UK | 46 | F | N | S, As |
| 59. | Orlandi *et al*. 2011 | Italy | 74 | F | N | N |
| 60. | Hong *et al*. 2012 | China | 39 | M | N | S |
| 61. | Ravi Parkash *et al*. 2012 | India | 57 | M | N | S, TB |
| 62. | Shubait *et al*. 2012 | Turkey | 51 | M | N | S, A |
| 63. | You *et al*. 2012 | Korea | 45 | M | Y | N |
| 64. | Akheel *et al*. 2013 | India | 49 | M | N | S, A |
| 65. | Arroyo *et al*. 2013 | Brazil | 64 | M | N | S |
| 66. | Hiraoka *et al*. 2013 | Japan | 80 | M | N | N |
| 67. | Paktas *et al*. 2013 | Turkey | 50 | F | Y | N |
| 68. | Ambroggi *et al*. 2014 | Italy | 54 | M | Y | NA |
| 69. | Amro *et al*. 2014 | Morocco | 66 | M | N | S |
| 70. | Bille *et al*. 2014 | Italy | 68 | M | Y | N |
| 71. | Ganesh *et al*. 2014 | India | 60 | M | Y | N |
| 72. | Ohnischi *et al*. 2014 | Japan | 62 | M | Y | NA |
| 73. | Oslen *et al*. 2014 | Victoria | 42 | M | N | MSP |
| 74. | Shi *et al*. 2014 | China | 61 | M | N | S |
| 75. | Debnath *et al*. 2015 | Bangladesh | 50 | M | N | NA |
| 76. | Kalastido *et al*. 2015 | Greece | 69 | M | N | NA |
| 77. | Kim *et al*. 2015 | South Korea | 77 | M | N | TB |
| 78. | Rajnikanth *et al*. 2015 | India | 62 | M | N | N |
| 79. | Sawaki *et al*. 2015 | Japan | 75 | M | N | S, As, HT |
| 80. | Shaikh *et al*. 2015 | USA | 58 | F | N | S. |
| 81. | Tajima *et al*. 2015 | Japan | 62 | M | Y | N |
| 82. | Tachibana *et al*. 2015 | Japan | 66 | M | Y | N |
| 83. | Arsnal *et al*. 2016 | Turkey | 59 | M | Y | NA |
| 84. | D- anito *et al*. 2016 | Italy | 76 | M | Y | S, PE, BH |
| 85. | Fukukoka *et al*. 2016 | Japan | 64 | M | N | S |
| 86. | Jeba *et al*. 2016 | India | 45 | M | N | S, DM |
| 87. | Lenouvel *et al*. 2016 | UK | 59 | M | N | N |
| 88. | Nakamura *et al*. 2016 | Japan | 79 | M | N | N |
| 89. | Nuyen *et al*. 2016 | USA | 59 | M | N | N |
| 90. | Sawheny *et al*. 2016 | USA | 52 | M | N | S, HT |
| 91. | Souren *et al*. 2016 | France | 70 | M | Y | S |

**Table 1 cont.-1**: Demographic data of patients with oral soft tissue metastasis from lung cancer as the sole primary source (1st August 1977 to 31st December 2021).

| | | | | | | |
|---|---|---|---|---|---|---|
| 92. | Unsal *et al*. 2016 | Turkey | 75 | M | N | S |
| 93. | Wang *et al*. 2016 | China | 56 | F | N | HT |
| 94. | Cheng *et al*. 2017 | China | 56 | M | N | S |
| 95. | Ito *et al*. 2017 | Japan | 85 | M | Y | N |
| 96. | Lawande *et al*. 2017 | India | 52 | M | N | S, A |
| 97. | Lee *et al*. 2017 | Korea | 63 | M | N | S, A |
| 98. | Thottian *et al*. 2017 | India | 37 | F | N | A |
| 99. | Valle *et al*. 2017 | USA | 61 | M | Y | MM |
| 100. | Wang *et al*. 2017 | USA | 73 | M | N | S |
| 101. | Gargouri *et al*. 2018 | Tunisia | 82 | M | N | S |
| 102. | Ishida *et al*. 2018 | Japan | 61 | M | N | N |
| 103. | Jihan *et al*. 2018 | Morocco | 57 | M | N | S |
| 104. | Abe *et al*. 2019 | Japan | 76 | M | N | S, As, AAE, CAF |
| 105. | Chen *et al*. 2019 | Taiwan | 75 | M | N | S, HT, GERD |
| 106. | Cui *et al*. 2019 | China | 64 | M | N | S |
| 107. | Ketadai *et al*. 2019 | Japan | 64 | M | N | HT, DM |
| 108. | Quin *et al*. 2019 | China | 63 | M | N | T |
| 109. | Tian *et al*. 2019 | China | 51 | F | NA | N |
| 110. | Tirkey *et al*. 2019 | India | 50 | M | Y | TB, RS, CVD |
| 111. | Tsai *et al*. 2019 | USA | 71 | M | Y | S, A, AF, COPD |
| 112. | Wang *et al*. 2019 | China | 70 | M | Y | S |
| 113. | Zaubitzer *et al*. 2019 | Germany | 66 | F | N | S |
| 114. | Devasse *et al*. 2020 | India | 61 | M | N | S, FNP |
| 115. | Lee *et al*. 2020 | Korea | 87 | F | N | N |
| 116. | Murakami *et al*. 2020 | Japan | 80 | M | N | N |
| 117. | Rocha *et al*. 2020 | Brazil | 55 | M | Y | S, A |
| 118. | Singh *et al*. 2020 | India | 60 | M | N | S |
| 119. | Yucell *et al*. 2020 | Turkey | 50 | M | Y | N |
| 120. | Guo *et al*. 2021 | USA | 70 | F | Y | AF, DVT,OA |
| 121. | Kuge *et al*. 2021 | Japan | 61 | M | N | N |
| 122. | Xu *et al*. 202*1* | China | 70 | M | N | S |

A: Alcohol, AAE: Abdominal aortic aneurysm, AF; Atrial fibrillation, As: Asbestos, BH: Bilateral hypoacusis, CAF: Chronic atrial fibrillation, CC: Cholecystectomy, CD: Crohon's disease, COPD: Chronic obstructive pulmonary disease, CRF: Chronic renal failure, CVA: Cardiovascular accident, DVT: Deep vein thrombosis, F: Female, FHOLC: Family history of lung cancer. FNP: Facial nerve palsy, GERD: Gastroesophageal reflux disease, IHD: Ischaemic heart disease, L: Left, M: Male, MI: Myocardial infarction, MM: Multiple myeloma, MSP: Musculoskeletal pain, N: No, NA: Not available, OA: Osteoarthritis, PE: Pleural effusion, RS: Rhinosporiodosis, S: Smoking, TB: Tuberculosis, Y: Yes

**Table 2**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| P. No. | Oral Site | C/C | Clinical presentation | Was it Initial site of metastasis? | Was it only site of metastasis? | Type of LC | Side of LC |
|---|---|---|---|---|---|---|---|
| 1. | G (Max, BL) | Swelling in upper gums since few days | Soft swelling | Y | Y | AD | NA |
| 2. | T (L, Ant 2/3rd) | Painful swelling in tongue | Painful swelling | Y | Y | AD | NA |
| 3. | SMG | Mass in submandibular region | Painful swelling | Y | Y | SCLC | NA |
| 4. | To (R) | Fever, dyspnoea, right tonsillar mass | Nonulcerated swelling | Y | N (Hilar LN) | AD | R |

**Table 2 cont.**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 5. | P (L) | Dry cough, left facial weakness | FNP, Tender nodule at angle of L Mand | Y | N (Li, Ad) | SCLC | L |
| 6. | To (L) | Cough, weight loss, short breath for 1 month | Large lobulated swelling, SMG Lymphadenopathy, | Y | N | SCLC | R |
| 7. | T (R, Post 1/3rd) | Swelling on tongue | Tongue swelling with ulceration | N (TNG) | N | SCC | R |
| 8. | G (Max, Post, L) | Routine exam | Soft growing swelling, ulcerated, BOP | N (2 Mon AD-OLC) | Y | AD | NA |
| 9. | P (BL) | Painless swelling of left face | Swelling in parotid region both sides | Y | Y | SCLC | R |
| 10. | P (L) | Painless swelling | Soft, tender, swelling | Y | N (Pituitary, SC) | SCLC | R |
| 11. | G (Mand, Post, R) | Haemoptysis | Pedunculated swelling | N (16 days ADOLC) | N (Adr, Inguinal) | AD | R |
| 12. | T (Lat border) | Swelling | Painful swelling | Y | Y | MT | NA |
| 13. | To (R) | Dry cough and spiking fever | Tonsillar mass on right side | N (1 Wk AD-OLC) | N (Right cervical LN) | LCLC | L |
| 14. | G (Max, Ant, BL) | Swelling in upper gums | Swelling, Generalized gingival inflammation | Y | Y | AD | NA |
| 15. | G (Mand, Post, L) | Swelling in lower jaw region | Hemorrhagic, soft, non-tender, well-demarcated swelling | Y | Y | MT | NA |
| 16. | G (Mand, L) | Swelling in lower gums | Soft, non-tender swelling | Y | Y | AC | NA |
| 17. | G (Max, R) | Swelling in upper gums | Soft, non-tender swelling | NA | NA | LCC | NA |
| 18. | G (Max, L) | Swelling in upper gums | Soft, non-tender swelling | NA | NA | LCC | NA |
| 19. | G (Mand, BL) | Swelling in lower jaw region | Soft, non-tender swelling | NA | NA | LCC | NA |
| 20. | G (Mand, R) | Bloody sputum and chest pain while coughing | Firm painful swelling, BOP. | Y | N (SNG) | LCC | L |
| 21. | G (Mand, L) | Gingival swelling | Soft, painful swelling, BOP | Y | Y | SCC | NA |
| 22. | UL | Pain in upper lip | Ulcerated nodule | N (TNG) | N (Skin) | MT | NA |
| 23. | T (DL) | Chronic bleeding from a nodular consolidation of tongue | Nodular, ulcerated, erythematous swelling | N (14 mon AD-OLC) | Y | MT | NA |
| 24. | P (L) | Painless swelling | Soft painless swelling | Y | Y | SCLC | NA |
| 25. | BM (R) | Painless swelling | Soft painless swelling | Y | N (Cervical) | MT | NA |
| 26. | T (L base and midline) | Painful lump on tongue for 2 months. | Painful non-ulcerated nodule, dysarthria, dysphagia | Y | N (B, Bone, Muscles) | SCC | R |
| 27. | P (R) | Pain in right facial region | Firm, painful swelling | Y | Y | SCLC (L) | NA |

**Table 2 cont.-1**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 28. | G (Max; Post, R& Ant L) | Right lung mass | Rapidly growing painful protruding masses, BOP | N (6 mon AD-OLC) | N (SNG) | AD | R |
| 29. | G (Max, Post, R) | Gingival swelling | Pedunculated, exophytic mass | N (Few days ADOLC) | Y | AD | NA |
| 30. | T (Lat border) | Swelling on tongue | Soft oedematous swelling | NA | NA | MT | NA |
| 31. | To (Ling) | Swelling in tonsillar region | Soft swelling | N (6 mon AD-OLC) | Y | AD | R |
| 32. | T (Ant 2/3rd) | Tongue swelling | Soft, mobile, submucosal mass | N (NA) | Y | MT | NA |
| 33. | G (Max, Ant, R) | Pain in column | Exophytic, nodular mass with ulcerated surface | N (2 mon AD-OLC) | N (Adr) | NSCLC | R |
| 34. | T (Ant) | Painful swelling on tongue | Painful, non-ulcerated nodule | N (TNG) | N (NA) | SCC | R |
| 35. | G (Mand, Ant, L) | Rapidly growing pedunculated exophytic mass on the gingiva at the left side of the lower jaw | Pedunculated, exophytic growth | Y | Y | Sa | L |
| 36. | G (SNA) | Gingival swelling | Soft swelling resembling, BOP PG | N (Few days ADOLC) | N (NA) | AD | NA |
| 37. | G (SNA) | Swelling | Firm, well demarcated swelling | Y | Y | NSCLC | NA |
| 38. | T (Ant) | Tongue swelling | Firm, well demarcated swelling | N (6 mon AD-OLC) | Y | MT | NA |
| 39. | To (L Palatine) | Foreign body mass | Reddish, fleshy, exophytic mass with area of necrosis and hemorrhage | N (2 Wk AD-OLC) | N (Li, Sp, Ri) | AD | L |
| 40. | G (Mand, R) | Painless swelling in lower gums | Red-greyish fungiform, centrally ulcerated mass | Y | Y | NSCLC | R |
| 41. | T (SNA) | Painful swelling on tongue | Painful mass without ulceration, dysarthria, dysphagia | Y | Y | AD | NA |
| 42. | G (Mand, L) | Rapidly growing, painless, exophytic mass in left post mand region | Rapidly growing, painless, exophytic mass | Y | N (SNG) | AD | L |
| 43. | G (Mand, Ant, R) | Dizziness | Red, smooth and easily bruised mass | Y | N (B) | AD | L |
| 44. | T (L dorsal) | Painful swelling on tongue | Nodular swelling | N (3 Yr. AD-OLC) | N (Skin) | MT | L |
| 45. | To (R Palatine) | Sore throat | Painless, soft, swelling | N (Appx 2 Yr ADOLC) | N (Li, Ab, Adr, B) | NEC | R |

**Table 2 cont.-2**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 46. | To (R Palatine) | Dysphagia and swallowing pain, with a foreign-like body sensation | White hard object within the right tonsillar crypt resembling tonsolith/ peritonsillar abscess. | N (6 mo ADOLC) | Y | SCLC | R |
| 47. | T (base) | Painful swelling on tongue | Swelling with deviation to left | Y | N (B, Skeleton) | AD | NA |
| 48. | LL | Dyspnoea since one week. | Ulcerated lesion with indurated margins | Y | Y | NSCLC | R |
| 49. | T (SNA) | Dysphagia, painful mass in right tongue | Non-ulcerative, hard, submucosal lump on the right postero-lateral aspect of the tongue | Y | N | AD | NA |
| 50. | FOM, , T, Ant tonsillar pillar | Rapidly growing right floor of mouth lesion for 3 weeks | Hard submucosal mass in the right FOM that extended 1 cm across the midline. | N (1 Yr. ADOLC) | N (Neck, Li, ri, SM) | MT | L |
| 51. | T (R Ant) | Swelling and pain of the tongue, and difficulty in breathing | Diffusely indurated swelling, overlying mucosa normal, mimicked abscess. | Y | Y | AD | R |
| 52. | G (Mand, Post, L) | Painful intraoral swelling on lower left posterior side of jaw since 20 days. | Reddish-pink, firm, pedunculated growth, associated with pus discharge, BOP, and sloughing. Mimicking PG, PGCG | Y | N (B) | AD | R |
| 53. | P (R ) | Painless mass in front of the mandible | Ulcerated painless mass | Y | N (B, V, Li) | SCLC | R |
| 54. | Multiple sites (G, AP, MS) | Painless sessile growth of size 2 × 3 cm on the lingual attached gingiva in relation to mandibular incisors of one month duration | Soft to firm swelling, no BOP, mobile anterior teeth, blanched nonulcerated overlying mucosa | Y | N (Adr) | AD | L |
| 55. | G (Mand, Post, L) | Gingival mass in the left side of lower jaw for 15 days | Pedunculated exophytic rapidly growing mass, BOP mimicking PG | Y | Y | AS | R |
| 56. | G (Max, Post, L) | Painless gingival mass | Swelling | Y | NA | SCLC | NA |
| 57. | G (Mand, Post, R) | Painless growth of the lower posterior attached gingiva for weeks. | Exophytic, firm, ulcerated mass | N (2 Yr. ADOLC) | Y | MT | R |
| 58. | T (L Post dorsum) | Routine check up | Firm, nodular polypoid, pink swelling with normal mucosa mimicking BFEP. | Y | Y | MT | L |

**Table 2 cont.-3**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 59. | G (Mand, Ant, R) | Swelling on lower gingiva | Swelling of vestibular gingival mucosa at the level of the lower right incisors | Y | Y | AD | R |
| 60. | To (R Palatine) | Dry cough for 7 moths. | Soft tissue swelling | N (3 mon AD-OLC) | Y | NSC LC | R |
| 61. | G (Max & Mand Ant, R Mand Post) | Multiple painless gingival swellings in the maxillary and mandibular gingiva since three months. | Soft, pedunculated, exophytic, erythematous and haemorrhagic tumefaction, Mimicking PG | Y | Y | AD | R |
| 62. | G (Mand Post, L) | Gingival mass | Ulcerated growth mimicking PG | N (8 mon AD-OLC) | N (Clavicle) | AD | L |
| 63. | G (Mand Post, L) | Gingival mass | Reddish-pink, soft to firm exophytic mass | N (8 mon AD-OLC) | Y | AD | L |
| 64. | Pa (L; Junc HP & SP) | Slow growing, painless, non-tender, firm swelling in the left side at the junction between hard and soft palate from past 2 months | Painless, non-tender, firm swelling | Y | Y | SCC | L |
| 65. | To (L Palatine) | Sore throat | Ulcerated lesion covered with fibrin | Y | Y | SCLC | L |
| 66. | G (Max, R) | Swelling | soft elastic mass | Y | N (Brain, stomach) | LCLC | L |
| 67. | G (Mand, Post, L) | Firm, hemorrhagic, tender swelling on the left mandibular bicuspid gingiva | Firm, haemorrhagic, tender swelling | N (6 mon AD-OLC) | Y | SCLC | L |
| 68. | SMG (R) | Routine chest check-up | Hypertrophy. | N (7 yr. ADOLC) | N (SNG) | MT | R |
| 69. | G (Max, Post, R) | Chest pain, weight loss, effort dyspnoea and fever. | soft tender swelling mimicking PG | Y | Y | AD | R |
| 70. | G (Mand Ant) | Painless growth of the lower attached gingiva for 4 weeks | Painless swelling | N (1.5 yr. AD-OLC) | N (Ad) | MT | L |
| 71. | T (L Lat border) | Swelling on tongue | Firm swelling | N (2 mon AD-OLC) | Y | Sa | L |
| 72. | G (Max, Post, L) | two-month history of progressive shortness of breath on exertion | Semi-hard, haemorrhagic lesion | N (1 mon AD-OLC) | Y | MT | L |
| 73. | G (Mand Ant, L) | Right shoulder pain | Firm, pedunculated lesion | N (TNG) | N (Li, B) | NSCLC | R |
| 74. | P (R) | Progressive painful swelling in the right parotid gland for one month | Non-tender swelling | Y | Y | AD | R |
| 75. | P (L) | Left facial swelling | Painless mass | Y | Y | AD | L |
| 76. | G (Mand Ant) | Swelling in lower front gum region | Soft exophytic lesion with pinkish white colour and irregular surface | N (TNG) | N (Ab) | NEC | NA |

**Table 2 cont.-4**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 77. | To (R Palatine) | dysphagia, painful mass in right tongue | Large oval mass | Y | N (Brain) | SCLC | BL |
| 78. | G (Max, Post, R) | Swelling in the right lower teeth region of the jaw for a month. | Polypoid, exophytic, asymptomatic lesion with an ulcerated growth, mimicking PG | Y | Y | AD | L |
| 79. | G (Max, Post, R) | Swelling in back tooth region | Swelling | Y | N (Intestine, Li, V, Ab, Pe) | MT | R |
| 80. | SMG (BL) | Cough | Bilateral swelling | Y | N (B) | SCLC | R |
| 81. | To (R Palatine) | Sore throat | Swelling | N (10 Yr ADOLC) | Y | SCC | R |
| 82. | G (Mand Post, L) | Swelling in lower left back region of jaw | Swelling, BOP | Y | Y | AD | L |
| 83. | RMT (R) | Rapidly growing painless growth at retromolar trigone area for 2 months | Soft, haemorrhagic, ulcerated lesion | N (2 yr. ADOLC) | N (V) | MT | L |
| 84. | To (R Palatine) | Dyspnoea, associated to strep throat and difficulty swallowing, | Swelling | Y | Y | SLCC | L |
| 85. | To (R Palatine) | Progressive shortness of breath, persistent cough with blood-streaked mucus, and hoarseness that had begun two months previously | Large ulcerated mass | Y | N (B) | SCLC | R |
| 86. | T (L Ant 2/3rd) | Dyspepsia, melena, symptoms due to anaemia and swelling in the tongue. | Swelling without ulceration, dysarthria, dysphagia, hoarseness. | Y | N (Duodenum) | AD | L |
| 87. | P (SNA) | Painful swelling on face | Preauricular mass | Y | Y | AD | BL |
| 88. | T (Tip) | Tongue swelling | Indurated swelling | Y | Y | NEC | L |
| 89. | G (Max, Ant, L) | Painful swelling | Swelling | Y | N (Li, Pe, Neck, V) | AD | R |
| 90. | G (Max, Ant) | Dyspnoea, left sided chest wall tenderness, intermittent productive cough, and weight loss. | Erythematous swelling | Y | Y | AD | L |
| 91. | G (Max Post, L) | Gingival hyperplastic lesion around tooth 27 | Swelling | N (18 mon ADOLC) | Y | NEC | L |
| 92. | To (L palatine) | Shortness of breath around a month | Swollen and oedematous tonsils. | Y | Y | SCLC | L |
| 93. | P (R) | Progressive painful swelling in the right parotid | Swelling with moderate texture and a normal local skin temperature. | Y | N (Cerebellum) | AD | L |
| 94. | T (Base) | Cough, fever, bloody sputum for 1 month | Non- ulcerated swelling | N (1Wk ADOLC) | Y | SCC | L |
| 95. | G (Max, Post, L) | Rapidly growing mass in buccal region for 1 week | Swelling. | N (1yr ADOLC) | N (B, Pan, Ad, Ki) | AD | L |

**Table 2 cont.-5**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 96. | P (R) | Right-sided gradually increasing facial swelling over the mandible over 11⁄2 months | Hard swelling with fixed skin overlying skin and no discharge | Y | N (Ab, Ki) | SCLC | R |
| 97. | T (Tip) | 2-week history of a mass on the tip of the tongue. | Demarcated, fungating and rubbery swelling | Y | Y | SCC | R |
| 98. | G (Max Post, L), HP | Dyspnoea and chest pain for two months. | Ulcero – proliferative lesions | N (2 mon AD-OLC) | N (Li) | SCC | L |
| 99. | To (L palatine) | Left-sided chest pain | Swelling | N (3.5 Yr ADOLC) | N (Li, CS, Ab) | HA | L |
| 100. | P (R) | 2-month history of progressive painful mass on the right upper face | Hard, fixed mass in the preauricular area | Y | Y | ACLC | R |
| 101. | G (Max, Post, R) | Gingival swelling for 2 months | Indurated and ulcerated polypoid mass | N (1 mon AD-OLC) | Y | AD | R |
| 102. | G (Max, R) | Painless gingival swelling for few days | Pedunculated mass resembling epulis | Y | N | AD | R |
| 103. | SMG (L) | 4-month history of a tumefaction in the left submandibular region that was slowly increasing in size, without any other associated signs. | Hard swelling | Y | N (Adr) | AD | R |
| 104. | Pa | Dry cough, left chest pain | Smooth small round mass | Y | Y | AD | L |
| 105. | To (L palatine) | Hemoptysis and mild productive cough for 2 weeks. | Exophytic growth with necrosis and haemorrhage | N (2 mon AD-OLC) | Y | AD | R |
| 106. | P (R) | Painless mass below the right ear and facial paralysis for a month. | Swelling, with poor mobility, FNP | Y | N (Neck) | SCLC | R |
| 107. | G (Max, Ant) | fever, cough | An indolent mass | Y | Y | NSCLC | L |
| 108. | G (Max,R) | Bloodstained sputum for a month. | Gradually increasing swelling, BOP | Y | Y | Sa | R |
| 109. | To (L palatine) | Discomfort and pain in throat for 20 days, | Mass with ulcers and necrosis | Y | N (Col, Li, Sp, Th) | AD | L |
| 110. | G (Max, Ant) | Swelling in upper front teeth | Pedunculated, erythematous, non-tender swelling without any pus discharge | Y | Y | NSCLC | NA |
| 111. | Pa (R) | Inability to wear his upper denture | Erosive, tender, lesion at the Junction of HP and SP | Y | Y | AD | R |
| 112. | G (Mand, R) | Gingival swelling | Soft tissue swelling with destruction of the mandible, and enlarged right submandibular lymph nodes | N (1.5 mon AD-OLC) | Y | Hepatoid A | R |

**Table 2 cont.-6**: Clinical details of patients with oral soft tissue metastasis from lung cancer (1st Aug 1977 to 31st December 2021).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 113. | To (R palatine) | Right-sided cervical lymphadenopathy and an asymmetry of the palatine tonsils | Indurated mass | Y | N (B) | AD | R |
| 114. | G (L Max Post) | Gingival mass | Reddish-pink dumbbell shaped pedunculated mass firm, asymptomatic ulcerated. | Y | N (Ri, V, Pe) | AD | L |
| 115. | SMG (L) | Difficulty in eating | Submandibular mass, intact FN | Y | Y | NEC | L |
| 116. | G (Mand, R) | Gingival mass | Tumor mass | Y | N (LN, Stomach) | Adenosqu | R |
| 117. | G (Mand, Ant) | Gingival swelling | Exophytic mass, with a smooth and lobulated surface, firm consistency | N (TNG) | Y | AD | NA |
| 118. | P (R) | Right sided facial swelling | Firm, lobulated, nontender mass fixed to the underlying structures, mobile overlying skin | Y | N (Scalp) | SCC | R |
| 119. | To (L) | Painful swelling on tongue | Asymmetric swelling, hypertrophic, necrotic resembling peritonsillar abscess | N (2.5 Yr AD-OLC) | N (Neck) | AD | NA |
| 120. | T (SNA) | Swelling | Oedematous T and FOM with normal underlying mucosa | Y | Y | P | NA |
| 121. | To (L Palatine ) | Sore throat for few days | Sore throat | N | N (Panc, Ad, Li, Brain) | Pl | R |
| 122. | To (L palatine) | Foreign body sensation in throat | Soft tissue mass | Y | Y | AD | L |

Ab: Abdomen, AC: Acinar cell carcinoma, AD: Adenocarcinoma, ADOLC: After diagnosis of lung cancer, ADOM: After diagnosis of metastasis, Adr: Adrenals, AFP: Anterior faucial pillar, Ant: Anterior, AS: Adenosquamous carcinoma, B: Bone, BL: Bilateral, BM: Buccal mucosa, BOP: Bleeding on probing, C: Cervical, Col: Column, CS: Cervical spine, DL: Dorsolateral, FNP: Facial nerve palsy, FOM: Floor of mouth, G: Gingiva, Ha: Hepatoid, HP: Hard palate, L: Left, LCC: Large cell carcinoma, M: Male, MS: Multiple sites, MT: Mesothelioma, N: No, NA: Not available, NEC: Neuroendocrine carcinoma, NG: Not given, NSCLC: Non-small cell lung carcinoma, P: Parotid, Pa: Palate, Pan: Pancreas, Pl: Pleomorphic, Pe: Pelvis, PG: Pyogenic granuloma, PGCG: Peripheral giant cell granuloma, Post: Posterior, R: Right, Ri: Rib, Sa: Sarcomatous, SCC: Squamous cell carcinoma, SCLC: Small cell lung carcinoma, SM: Skeletal muscles, SMG: Submandibular gland, SNG: Site not given, Sp: Spine, SP: Soft palate, T: Tongue, To: Tonsil, Th: Thorax, V: Vertebrae, Y: Yes.

**Table 3**: Data describing treatment and prognosis of patients with oral soft tissue metastasis from lung cancer (1st August 1977 to 31st December 2021).

| P. No. | Treatment given | Prognosis | Reason of death |
|---|---|---|---|
| 1. | C, R | NA | NA |
| 2. | R | Died during Tt | NA |
| 3. | S | NA | NA |
| 4. | C | D (25 days ADOM) | Dyspnoea, RF, CF |
| 5. | C, R | Fav | - |
| 6. | R | D (TNG) | NA |
| 7. | Died before Tt | D (28 mo ADOM) | NA |

**Table 3 cont.**: Data describing treatment and prognosis of patients with oral soft tissue metastasis from lung cancer (1st August 1977 to 31st December 2021).

| | | | |
|---|---|---|---|
| 8. | NA | NA | NA |
| 9. | C | D (3 Mon ADOM) | MM |
| 10. | C, R | D (TNG) | MM |
| 11. | R | D (3 mon ADOM) | MM |
| 12. | NA | NA | NA |
| 13. | C, R | Fav | - |
| 14. | NA | NA | NA |
| 15. | S | NA | NA |
| 16. | C, R | D (2.5 mon ADOM) | PE |
| 17. | C, R | D (3 mon ADOM) | NA |
| 18. | C, R | D (Appx 4 mon ADOM) | NA |
| 19. | C, R | D (Appx 4 mon ADOM) | NA |
| 20. | C, R | D (Appx 4 mon ADOM) | MM |
| 21. | R | D (2 mon ADOM) | NA |
| 22. | S | NA | NA |
| 23. | C, R | NA | NA |
| 24. | R | Fav | - |
| 25. | C | Fav | - |
| 26. | C, R | D (5 mon ADOM) | MM |
| 27. | S | NA | NA |
| 28. | S | D (2 mon ADOM) | MM |
| 29. | S | D (1 mon ADOM) | DC |
| 30. | NA | NA | NA |
| 31. | S | Fav | - |
| 32. | C, R | NA | NA |
| 33. | S | D (1 mon ADOM) | CRF |
| 34. | C | LFU | - |
| 35. | C | Fav | - |
| 36. | NG (due to MM) | D (TNG) | MM |
| 37. | C, R | NA | NA |
| 38. | R | Fav | - |
| 39. | C, R, S | D (1 Wk. ADOM) | Lack of full Tt. |
| 40. | C, R | Fav | - |
| 41. | C | NA | NA |
| 42. | S | NA | NA |
| 43. | NG | D (4 mon ADOM) | ALF |
| 44. | C | NA | NA |
| 45. | C | D (4 mon ADOM) | MM |
| 46. | C, R | Fav | - |
| 47. | C, R, S | D (9 mon ADOM) | MM |
| 48. | C | NA | NA |
| 49. | C, R | D (2 mon ADOM) | NA |
| 50. | S | D (2 mon ADOM) | MM |
| 51. | RTO | D (2 mon ADOM) | NA |
| 52. | NG due to ALF | D (1 wk. ADOM) | DC |
| 53. | C, Supp | NA | NA |
| 54. | C | D (9 mon ADOM) | MM |

**Table 3 cont.-1**: Data describing treatment and prognosis of patients with oral soft tissue metastasis from lung cancer (1st August 1977 to 31st December 2021).

| | | | |
|---|---|---|---|
| 55. | NG due to seizures | D (1.5 mon ADOM) | Seizure |
| 56. | C, R | NA | NA |
| 57. | C | NA | NA |
| 58. | C, R, S | TGO | - |
| 59. | C, R, S | D (1.5 mon ADOM) | RF |
| 60. | C | Not regressed | LFU |
| 61. | NA | D (1 mon ADOM) | CPF |
| 62. | C, R | D (2.5 mon ADOM) | RF |
| 63. | NG | D (1 mon ADOM) | DC |
| 64. | RTO | D (TNG) | MM |
| 65. | NG | D before Tt | NA |
| 66. | C, R | D (TNG) | Stroke |
| 67. | C | Recurrence LFU | - |
| 68. | R | NA | NA |
| 69. | C, S | D (TNG) | NA |
| 70. | C, R | NA | NA |
| 71. | RBP | - | - |
| 72. | S | D (4 mon ADOM) | DC |
| 73. | RBP | D (TNG) | MM |
| 74. | S, C, R | D (4 mon ADOM) | MM |
| 75. | NA | NA | NA |
| 76. | NG | D (2.5 Yr. ADOM) | MM |
| 77. | C | D (3 mon ADOM) | BM |
| 78. | C, R | TGO | - |
| 79. | R | Fav | - |
| 80. | C, R | LFU | - |
| 81. | Sy | NA | NA |
| 82. | NG | D (3 mon ADOM) | DC |
| 83. | NG | D (1.5 mon ADOM) | MM |
| 84. | C | D (11 mon ADOM) | DC |
| 85. | C | D (1 Yr. ADOM) | MM |
| 86. | C | LFU | - |
| 87. | S | LFU | - |
| 88. | C | NA | NA |
| 89. | R | NA | - |
| 90. | C, R | D (4 mon ADOM) | DC |
| 91. | C, R | D (1 Yr. ADOM) | DC |
| 92. | C | D (2 mon ADOM) | DC |
| 93. | C | UFU | - |
| 94. | C | D (12 mon ADOM) | DC |
| 95. | R | D (TNG) | Cachexia |
| 96. | C, R | D (TNG) | MM |
| 97. | S, C | D (8 mon ADOM) | DC |
| 98. | C, R | D (1 mon ADOM) | DC |
| 99. | R | D (1 Yr. ADOM) | MM |
| 100. | C | TGO | - |
| 101. | R | D (2 mon ADOM) | DC |

**Table 3 cont.-2**: Data describing treatment and prognosis of patients with oral soft tissue metastasis from lung cancer (1st August 1977 to 31st December 2021).

| | | | |
|---|---|---|---|
| 102. | R, C | D (3 mon ADOM) | PH |
| 103. | C, R | Fav | - |
| 104. | C | D (4 mon ADOM) | DC |
| 105. | S, Ta | Fav | - |
| 106. | C, Su | Fav | - |
| 107. | C | D (TNG) | RDS |
| 108. | C, R | D (2 mon ADOM) | MM |
| 109. | C, Ta | D (5 mon ADOM) | DC |
| 110. | RTO | LFU | - |
| 111. | RTO | LFU | - |
| 112. | R | D (9 mon ADOM) | DC |
| 113. | C, R | Fav | - |
| 114. | Palliative, C, R suggested. | D (2 mon ADOM) | MM |
| 115. | NG | D (3 mon ADOM) | LFA |
| 116. | C | D (TNG) | DC |
| 117. | Died before Tt | D (1mon ADOM) | RF |
| 118. | C, R | D (9 mon ADOM) | DC |
| 119. | S | D (10 mon ADOM) | RF |
| 120. | S, C | TGO | - |
| 121. | C, R | TGO | - |
| 122. | C | Fav | - |

ADOM: After diagnosis of metastasis, ALF: Acute lung failure, BM: Brain metastasis, C: Chemotherapy, CPF: Cardiopulmonary failure, D: Death, DC: Deteriorated condition, Fav: Favourable, IHD: Ischaemic heart disease, LFA: Liver function abnormality, LFU: Lost to follow up, MM: Multiple metastasis, mon; Months;, NA: Not available: NG: Not given, PE: Pleural effusion, PH: Pulmonary haemorrhage, RBP: Refused by patient, RF: Respiratory failure, RDS: Respiratory distress syndrome, RTO: Referred to oncologist, S: Surgery, Su: Supportive, Sy: Symptomatic, Ta: Targetoid, TGO: Treatment going on, Tt: Treatment, UFU: Under follow up; Wk: Weeks; Yr: Years.

**Table 4**: Summary of results documented from literature research describing the characteristics of oral soft tissue metastasis from lung cancer (1st August 1977-31st Decemebr 2021).

| Feature | Number |
|---|---|
| Total number of papers published | 120<br>CR-111<br>SC-3<br>LTE-3<br>Co-2<br>RA-1 |
| Total number of patients | 122 |
| World-wide distribution of cases | Japan (31) 25.8%<br>India (14) 11.7%<br>USA (13) 10.8%<br>China (10) 8.3%<br>Turkey (9) 7.5%<br>Italy (7) 5.8%<br>Korea= UK (5) 4.2%<br>Brazil (4) 3.3%<br>Morocco=Taiwan=France=Greece=Tunisia=Germany=<br>Switzerland= Australia =Spain (2) 1.7%<br>Israel=Beirut =Bangladesh=Victoria (1) 0.8% |
| Gender | M -100 (82%)<br>F- 22 (18%) |
| Average age of patients (Range) | 60.8 Years. (25-87 Years) |
| Average age of male patients (Range) | 61.4 Years. (25-87 Years.) |

**Table 4 cont.**: Summary of results documented from literature research describing the characteristics of oral soft tissue metastasis from lung cancer (1st August 1977-31st Decemebr 2021).

| | |
|---|---|
| Average age of female patients (Range) | 58.3 Years. (36-87 Years) |
| Chief complaint | Related to oral health -97 (79.5%)<br>Not related to oral health -22 (18%)<br>Routine check-up-3 (2.5%) |
| Previous history of LC | 35 (28.7%) |
| No previous history LC | 78 (63.9%) |
| NA data of previous history of LC | 9 (7.4%) |
| Associated risk factors | 66 (54.1%)<br>S-53 (80.3%)<br>A-9 (13.6%)<br>HT-7 (10.7%)<br>As-6 (9.1%)<br>TB-3 (4.5%)<br>Others 15 (27.2%) |
| No risk factors | 38 (31.1%) |
| NA data of associated risk factors | 18 (14.8%) |
| Site of metastasis | G -51 (41.8%)<br>(Max-24, (47%) Mand-25, (49%) SNA-2 (4%)<br>Max- (Ant-6, Post-12,Both-1, SNA-5)<br>(R- 10, L-5, Both-4, SNA-5)<br>Mand-(Ant-6, Post-9, Both-2, SNA-8),<br>(R-8, L-12, Both-2, SNA-3)<br>T- 21 (Ant-6, Base-4, DL-6, SNA-3, Tip-2) 17.2%<br>To – 21 (Palatine-19 (R-10, L-9), Lingual-2) 17.2%<br>P – 14 (R-8, L-4, BL-2) 11.5%<br>SMG -5 (L-3, R-1, BL-1) 4.1%<br>Pa- 3 (2.5%)<br>Lip- 2 (U-1, L-1) 1.6%<br>BM-1 0.8%<br>RMT-1 0.8%<br>MS -3 (2.5%) |
| Oral soft tissues as the initial site of metastasis | Y- 74 (60.6%)<br>N-44 (36.1%)<br>NA-4 (3.3%) |
| Oral soft tissues as the only site of metastasis | Y-63 (51.6%)<br>N-54 (44.2%)<br>NA-5 (4.2%) |
| Average time of detection of metastasis from diagnosis of LC | Few days to 10 Years. |
| Most common clinical features | Swelling (100) 81.9%<br>Ulcerated (13) 10.6%<br>Exophytic (12) 9.8%<br>Pedunculated (10) 8.2%<br>Nodular (6) (4.9%)<br>Odema (5) (4.2%)<br>Erosive (2) (1.6%)<br>BOP (10) 8.2%<br>ST =LP=FNP (1) (0.8%) |
| Type of LC | AD (46) 37.7%<br>SCLC (19) 15.6%<br>MT(17) 13.9%<br>SCC (10) 8.2%<br>NSCLC (8) 6.5%<br>LCC (6) 4.9%<br>NEC (5) 4.1%<br>Sa (3) (2.4%)<br>Ha (2) 1.6%<br>AC (2) 1.6%<br>AS (2) 1.6%<br>Pl (2) 1.6% |

**Table 4 cont.-1**: Summary of results documented from literature research describing the characteristics of oral soft tissue metastasis from lung cancer (1st August 1977-31st Decemebr 2021).

| | |
|---|---|
| LC Metastasis | IL-55 (45.1%)<br>CL-33 (27%)<br>BL-2 (1.6%)<br>NA-32 (26.2%) |
| Treatment aids | RT+CH (31) 25.4%<br>CH (27) 22.1%<br>RT=SU (12) 9.8%<br>CH+RT+SU (8) 6.5%<br>CH+SU (2) 1.6%<br>SU+ Ta =SU=Sy (1) 0.8%<br>NG(11) 9%<br>NA(5) 4.1%<br>RBP (4) 3.3%<br>STO (2) 1.6% |
| Death | 66 (54.1%) |
| Reasons of death | MM (18) 27.2%<br>DC (18) 27.2%<br>RF (4) 6.1%<br>Others (13) 19.7%<br>NA (13) 19.7% |
| Average time of death from diagnosis of Metastasis | 1 Week- 2.5 Years |
| Partial relief of symptoms | 1 (0.8%) |
| Favourable prognosis | 13 (10.6%) |
| TGO | 5 (4.1%) |
| LFU | 6 (4.9%) |

A: Alcohol, AC: Acinar cell carcinoma, AD: Adenocarcinoma, AFP: Anterior faucial pillar, Ant: Anterior, AS: Adenosquamous carcinoma, As: Arsenic, BL: Bilateral, BM: Buccal mucosa, BOP: Bleeding on probing, CH: Chemotherapy, CL: Contralateral, Co: Correspondence, CR: Case report, DL: Dorsolateral, F: Female, FOM: Floor of mouth, G: Gingiva, Ha: Hepatoid, HT: Hypertension, IL: Ipsilateral, L: Left, LC: Lung cancer, LCC: Large cell carcinoma, LFU: Lost to follow up, M: Male, MS: Multiple sites, MM: Multiple metastasis, MT: Mesothelioma, N: No, NA: Not available, NEC: Neuroendocrine carcinoma, NG: Not given, NSCLC: Non-small cell lung carcinoma, P: Parotid, Pa: Palate, Pl: Pleomorphic, Post: Posterior, R: Right, RA: Retrospective analysis, RBP: Refused by patient, RF: Respiratory failure, RMT: Retromolar triagone, S: Smoking, Sa: Sarcomatous, SC: Short communication, SCC: Squamous cell carcinoma, SCLC: Small cell lung carcinoma, SMG: Submandibular gland, SNA: Site not available, ST: Sore throat, STO: Sent to oncologist, SU: Surgery, Sy: Symptomatic, T: Tongue, TB: Tuberculosis, To: Tonsil, TGO: Treatment going on; Y: Yes

(6). In our study, 80% cases had habit of smoking. Asbestos-induced inflammation has been found to promote the neoplastic transformation of mesothelial cells leading to development of LC, particularly mesothelioma (7,8). In the present research appx 9% patients had a history of asbestos exposure.

People with underlying comorbidities are more likely to acquire cancer and have a worse prognosis as a result of distant metastasis induced by a weakened immune system. 27.2% patients in this study had a variety of underlying comorbidities, the most prevalent of which were cardiac, respiratory, and renal.

The incidence of oral metastatic lesions is not so specific in any region of the world. In our study, the maximum number of cases were from Japan (n-31), followed by India (n-14), and USA (n-13), Various other regions were also involved (table 4). Looking at this data, wide region involvement of OSTM from LC can be appreciated.

The most common site of OSTM is the attached gingiva (57%), followed by the tongue (27%), tonsil (8%), palate (4%), lip (3%), Buccal mucosa (1%), and floor of mouth (<1%) (9). In the present research also, some similar results were observed with maximum cases found on gingiva >tongue = tonsils.

Pathogenic mechanisms of OSTM aren't completely understood. Metastasis is a multistage process that involves tumour cells being detached from their originating site and being transported to a secondary site via lymphatic or hematogenous channels (10). One of the proposed pathways is the "Batson's plexus," a valveless prevertebral venous plexus network that involves retrograde tumour cell movement from the lungs to the face. Another pathway of metastasis in LC involves direct suction, access to the pulmonary vein, and drainage to the left side of the heart (11).

Chronically, inflamed mucosa in the oral soft tissues,

particularly attached gingiva, contains a dense capillary network that can trap malignant cells and promote metastases. On the other hand, some reports of metastases to the post-extraction site suggest that local variables in the extraction or wound area may attract circulating tumour cells. Because tooth extraction generates a milieu rich in growth factors, it may promote metastasis. The extraction site of a tooth is thought to be a microenvironment rich in local growth factors that encourage metastatic cell development (9).

Studies conclude that gingival metastasis mostly occurs in mandibular area than maxillary with predominancy of posterior side involvement (5,9,10). In the current research however, there was almost equal involvement of maxillary and mandibular gingiva. Posterior region was predominantly affected than anterior region. OSTM usually occurs unilaterally. In our research, left side predominated as compared to right in the mandibular gingiva, while maxillary gingiva showed right side predominance. 2 cases showed BL involvement each in mandible and 4 in maxilla.

The tongue is also a highly circulatory organ, which creates ideal conditions for the spread of cancer. According to a study, the lung was the second most common primary site metastasized to the tongue (5). The literature rarely mentions LC metastases to the tongue (12-14). In the present research, we could find 21 cases of tongue metastasis from LC. Posterolateral and dorsal part are more often involved in metastasis due to rich capillary and lymphatic network and immobility. On contrary, in the present research most of tongue metastasis was observed in anterior and dorsolateral region and base.

Tonsil metastasis has been reported to be extremely infrequent among oral soft tissues. Only 0.8 percent of 1535 cases of malignant palatine tonsillar tumours were metastases from an extra-tonsillar source, according to a study (15). In the current literature, 21 cases of tonsillar metastasis from LC have been observed and 19 of them were palatine tonsils. Only 2 cases occurred in lingual tonsil. Lymphatic spread to tonsils is rare due to lack of afferent lymphatic capillaries except retrograde spread via cervical lymph nodes or direct spread.

Metastatic deposits in the parotid gland from tumours outside the head and neck region are uncommon, but they have been recorded from lung, breast, and kidney cancers. These primaries account for roughly 10%–20% of all parotid secondary tumours (16). The abundant lymphatic flow seen in and around the gland parenchyma is most likely to blame for the dissemination to lymph nodes. Literature has revealed very rare number of cases of LC metastasis to parotid (17-18). In the current research out of 122 cases, only 14 involved parotid gland. Metastasis to other salivary glands such as submandibular gland, and sublingual gland is very rare. Owing to the lack of lymph nodes in these glands, route of metastasis is predominantly completely haematogenous. In our research, only 5 cases of submandibular gland metastasis from LC have been documented, while no case involved the sublingual gland.

The most common malignant neoplasms of the palatal mucosa are known to be minor salivary gland tumors (19). and metastatic tumors from a distant organ in this region is uncommon. In the present research, out of 122 cases of LC metastasis, only 3 were found in the palate region. Lip metastasis from distant resources is rarely documented in the literature. Few cases have been reported from colon and gastric cancers (20-21). In the present review, only 2 cases of lip metastasis from LC were notified. Floor of mouth and buccal mucosa are other rare sites of cancer deposits. Thin and movable mucous membrane in the floor of mouth region allows easy entrapment of tumour cells. In the present research, only one case of buccal mucosa and floor of mouth metastasis from LC was diagnosed.

Clinically, OSTM tumours grow rapidly causing pain, difficulty in chewing, dysphagia, disfigurement, and bleeding on probing . These metastatic lesions are often difficult to diagnose because their variable features such as polypoid or exophytic, highly vascularized growths or swelling, bear close resemblance to some benign hyperplastic or reactive oral lesions. Biopsy becomes mandatory to identify the exact primary source of metastasis. In present research, swelling was the most predominant clinical feature observed (81.9%). Other lesions appeared as ulcerative, exophytic, pedunculated, nodular, edematous, and erosive.

A history of LC could help in the detection of secondary metastatic cancer. Before the metastatic spread to the oral cavity, the majority of patients are aware of their primary tumours. However, metastasis to oral soft tissue via LC is a late indication. Only 35 of the patients in this research were aware of previous LC, whereas the other 78 had no such history.

Oral metastatic tumours are of high clinical importance because, they may be the only symptom of an undiagnosed underlying malignancy or the first sign of the metastasis. In our study,74 patients had evidence of metastasis as the initial symptom of the disease, whereas in 44 cases, metastasis was detected after the diagnosis of LC with an average time of few days to 10 years.

Histopathological examination is required to provide a conclusive diagnosis of the type of metastatic lesion. However, it might be difficult to make an exact diagnosis because these lesions have a varied histological appearance rather than a distinct picture. When the major focus of the primary metastatic site is known, diagnosing the secondary metastasis can be simple. Other tools, such as special staining, immunohistochemistry, and electron microscopy, may be necessary in some circumstances to determine the initial tumor's nature.

LC has been divided into subgroups based on histopathology. Many new entities have recently been introduced to the 2015 World Health Organization classification system (22). Adenocarcinoma has been discovered to be the most prevalent kind of LC that metastasizes to the oral soft tissues. And same was the finding in this study as well.

Although LC entails multiorgan distant metastases, oral soft tissues might occasionally be the only site of metastasis. Out of 122 instances in this study, 63 had oral soft tissues as the only location of LC metastasis, whereas 54 had metastasis to other parts of the body as well such as brain, kidney, adrenal, liver, vertebrae, spine, pelvis, skin, and skeletal muscles.

Treatment and prognosis of oral metastatic lesions are determined by the site of genesis and the extent of the disease. Treatment options include biopsy, surgery, chemotherapy, radiotherapy, brachytherapy, and/or combination therapy. The most commonly used therapy aids in this study were chemotherapy and radiotherapy. Combination therapy was also used in many cases. Unfortunately, OSTM by LC has a bad prognosis with a maximum survival rate of 5 years. In some cases, a patient's terminal stage of disease results in a loss of follow-up or, death. Even after treatment, 66 people died, according to the current study. The duration between death and oral metastasis diagnosis ranged from 1 week to 2.5 years. Multiple metastasis, deteriorated systemic condition, pleural effusion, and acute lung failure were the most common causes of death. 15 patients had a good prognosis with no signs of recurrence.

## Limitations of the current study

One of the limitations of current research was involvement of only individual based studies such as case reports and case series. We could find a very few large-scale studies related to the subject in our search. Studies such as epidemiological, case control, cohort, etc. were excluded, because we also aimed to evaluate individual features of these metastatic lesions. And in those studies, individual data of patients was not available.

## Conclusions

During the last 44 years (Aug 1977-Dec2021), we found only 122 cases of OSTM rom LC as the sole primary source. This signifies a rare occurrence of OSTM from LC. The prognosis was poor involving 66 deaths out of 122 cases with a survival rate of 1 week to 2.5 years. Gingiva, Tongue and tonsils were the most prevalent oral soft tissues to get metastasized. Because of their resemblance to other pathologies, and late clinical signs, these lesions go unnoticed the majority of the time. Diagnosis of oral metastatic lesions is a challenging task for the clinicians, and pathologists. A thorough examination of the metastatic lesions is required, including a review of the patient's medical history, clinical presentation, and early diagnosis in order to identify the primary site of metastasis and choose the best course of treatment. More cases need to be published in order to raise awareness of these lesions and gain a better understanding of their characteristics.

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**Abbreviations**
JB: Jaw bones, JBM: Jaw bone metastasis, LC: Lung cancer, NA: Not available, OST: Oral soft tissues, OSTM: Oral soft tissue metastasis, PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.