

Breast cancer metastasizing to salivary glands: Systematic review

ABSTRACT

Distant metastasis to salivary glands is a very rare event and most often associated with primary malignancies of the skin. Only 1-4% of all salivary gland tumours manifest with metastasis. Carcinomas of the breast, lung, kidney and prostate are those primaries that may also potentially metastasize to salivary glands. Literature has documented several studies analysing metastatic tumours in the oral region. However, very little research work has been published to date to analyse solely the Breast cancer metastasizing to the salivary glands. Thus, this review was conducted to examine the published cases of Breast cancer metastasizing to salivary glands from March 1975 to March 2023. An electronic search of the published literature was performed without publication year limitation in PubMed/ Medline, Scopus, Google Scholar, Web of Science, Science Direct, Embase, and Research Gate databases, using mesh keywords like ('Breast cancer' OR 'Breast carcinoma') AND ('Metastasis' OR 'Metastases'), And ('Salivary glands' OR 'Parotid gland' OR 'Submandibular gland' OR 'Sublingual gland'). We also searched all related journals manually. The reference list of all articles was also checked. Our research revealed a total of 48 relevant papers with 55 patients. Parotid was the most predominantly affected salivary gland. 14.5% of patients died with a mean survival time of 7 months. It can be concluded from this research that Breast cancer metastasizing to salivary glands is a rare occurrence. Careful evaluation of these cases is needed in order to raise awareness of these lesions and gain a better understanding of their characteristics.

Keywords: Breast cancer, metastasis, salivary glands

INTRODUCTION

Distant metastasis to salivary glands (SG) is very uncommon and most often associated with primary malignancies of skin. Only 1-4% of all salivary gland tumours (SGT) manifest with metastasis.^[1] Carcinomas of the breast, lung, kidney, and prostate are those primaries that may also potentially metastasize to SG. Breast cancer (BC) is the most common cause of death in the female population including cervical cancer. Worldwide, approximately 2.3 million new cases of BC and 684996 deaths due to this malignancy were recorded in 2022 according to GLOBACON databases^[2] and metastasis is the prime cause of death. The rate of metastasis even in uncommon sites is on the rise. On other side, it has been observed that the overall survival of BC patients has been prolonged owing to the more effective therapy and the development of new imaging techniques and early detection. The most common

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organs involved in distant metastasis of BC are bones, lungs, liver, and brain.^[3] SG is one of the rarest sites of metastasis from BC and parotid is the most common SG involved as reported first by Abrams *et al.*,^[4] in 1950 in a review of autopsy studies of 167 cases of BC, in which only 1 case of metastasis to the parotid gland was detected. Literature has documented several studies analyzing the metastatic tumors to the oral region.^[5-8] However, a very little research work has been published to date to analyze solely the BC metastasizing to the SG. Thus, this review was conducted to examine the published cases of BC metastasizing to SG in the literature from March 1975 to March 2023 and to learn about their characteristics.

MATERIALS AND METHODS

The current research was carried out following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Owing to nature of the current review, any ethical approval was not required.

Focused question

To conduct the study, context, condition, population (CoCoPop) framework, designed by Joanna Briggs Institute,

was used focusing on the research question ‘How many cases of BC metastasizing to SG have been documented in the literature, and what is the prognosis of these metastatic lesions?’

Pop (Population): Patients with BC

Co (Condition): Salivary gland metastasis

Co (context): Characteristics of these patients

Search strategy for identification of studies

An electronic search of the published literature was performed without publication year limitation in PubMed/Medline, Scopus, Google Scholar, Web of Science, Science direct, Embase, and Research gate databases, using mesh keywords like (‘Breast cancer’) AND (‘Metastasis’ OR ‘Metastases’), And (‘Salivary glands’ OR ‘Parotid gland’ OR ‘Submandibular gland’ OR ‘Sublingual gland’). We also searched all related journals manually. The reference list of all articles was also checked [Figure 1].

Screening of studies

The current review involved three steps of screening the studies. In the first step, titles were reviewed by two authors (SG, MMS) independently and duplicates were removed.

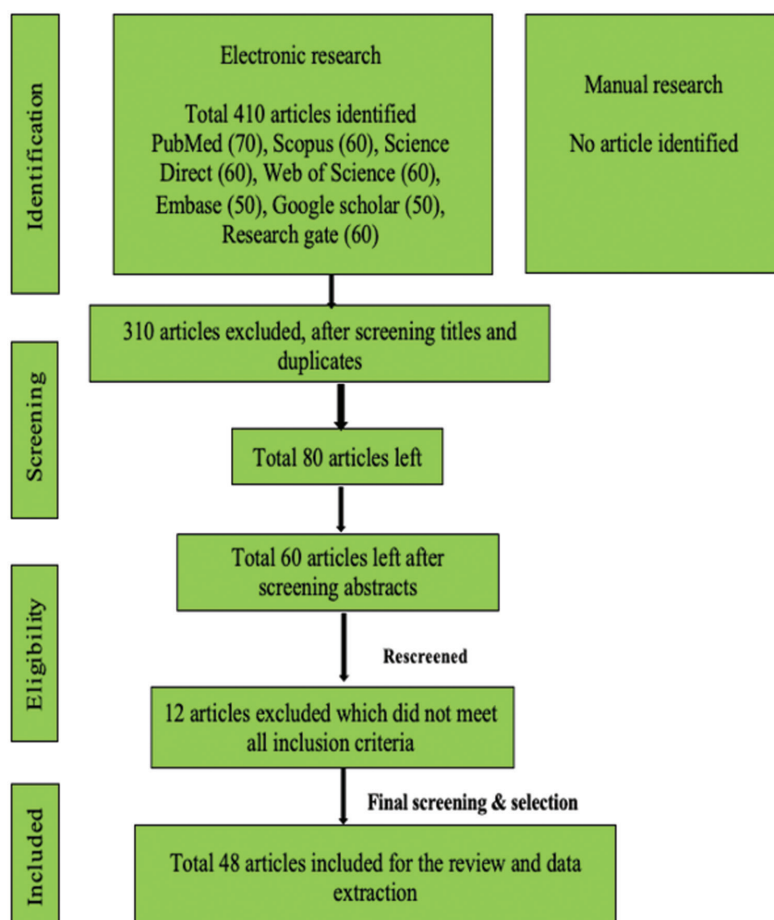


Figure 1: PRISMA Flowchart showing search strategy

Then the other four authors (MP, AEN, PS, NA) reviewed the selected abstracts of all the reports independently. The reviewers were calibrated on the basis of their assessment of their titles and abstracts of the first 50 references retrieved. The kappa value of agreement between reviewers was 0.83. If the title/ abstracts met the eligibility rule, they were included in the study. In the final stage, the text of selected studies was screened by remaining three authors (KQ, MEMH, ABY) separately. The 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 BC metastasizing to SG. The papers included were from March 1975 to March 2023.
- Type of studies: Case reports, Retrospective analysis and Original research.
- Cases were selected beyond the restriction of limitations on parameters such as age, ethnicity or socioeconomic status, etc.
- Articles published in any language were included.

Exclusion criteria

- Cases with no definite diagnosis of BC metastasizing to SG.
- Publications reporting the SG metastasis from any site other than the Breast.
- Cases with BC metastasizing to jaw bones and other oral soft tissues were not included.
- Studies which did not provide individual patient data were excluded.
- Editorials, conference abstracts, hypothesis papers, web news, media reports, and animal studies.

Data extraction and analysis

After study selection, screening, and a thorough examination, the data were extracted. The information gathered was cross-checked and tabulated into three tables [Tables 1-3]. 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. The results were expressed in descriptive statistics. The overall survival rate was calculated by survival analysis with Kaplan–Meier curves.

RESULTS [TABLE 4]

Our research strategy revealed 48 relevant papers.^[9-56] Papers included were from March 1975 to March 2023. A total of 55 patients included, all being females. The maximum number of cases were from the United Kingdom -UK (n-13) followed by India (n-6) and United States of America -USA (n-4).

Table 1: Details of publications reporting cases of Breast cancer metastasizing to Salivary glands (March 1975–March 2023)^[9-56]

S.no.	Authors	Type of study	Year	Country	No. of patients
1.	Solomon <i>et al.</i>	CR	1975	USA	1
2.	Meyers and Olshok	CR	1981	USA	1
3.	Wiesel <i>et al.</i>	CR	1982	Israel	3
4.	Rosti <i>et al.</i>	CR	1985	UK	1
5.	Bissett <i>et al.</i>	CR	1989	UK	2
6.	Calvo Boizas <i>et al.</i>	CR	1995	Spain	1
7.	Vessecchia <i>et al.</i>	CR	1995	Italy	1
8.	Bochnia <i>et al.</i>	CR	1997	Poland	1
9.	Kollias and Gill	OR	1997	UK	3
10.	Joycee <i>et al.</i>	CR	2000	Ireland	1
11.	Cain <i>et al.</i>	OR	2001	UK	1
12.	Szymanski <i>et al.</i>	CR	2002	Poland	2
13.	Zhang and Gu	CR	2003	USA	1
14.	Nuyens <i>et al.</i>	RA	2006	UK	2
15.	Perez-Fidalgo <i>et al.</i>	CR	2007	Spain	1
16.	Laforga and Gasent	CR	2008	Spain	1
17.	Dangore-Khasbage <i>et al.</i>	CR	2009	India	1
18.	Ramesh <i>et al.</i>	CR	2010	India	1
19.	Ando <i>et al.</i>	CR	2011	Japan	1
20.	Cihan <i>et al.</i>	CR	2011	Turkey	1
21.	Erra and Costamagna	CR	2011	Italy	1
22.	Sellinger <i>et al.</i>	CR	2011	Germany	1
23.	Alath <i>et al.</i>	RA	2014	Kuwait	1
24.	Akcan <i>et al.</i>	CR	2015	Turkey	1
25.	Duncan <i>et al.</i>	CR	2015	UK	1
26.	Murhekar <i>et al.</i>	CR	2015	India	1
27.	Khuranna <i>et al.</i>	CR	2016	India	1
28.	Kmeid <i>et al.</i>	CR	2016	Lebanon	1
29.	Srinivasan	CR	2016	USA	1
30.	El M'rabet <i>et al.</i>	CR	2017	Africa	1
31.	Franzan <i>et al.</i>	RA	2017	Germany	1
32.	Rewat <i>et al.</i>	CR	2017	UK	1
33.	Bohli <i>et al.</i>	CR	2018	Tunisia	1
34.	Cao <i>et al.</i>	CR	2018	China	1
35.	Aggarwal <i>et al.</i>	CR	2019	India	1
36.	Assarian <i>et al.</i>	CR	2019	Iran	1
37.	Cengiz <i>et al.</i>	CR	2019	Turkey	1
38.	Jakharia-Shah <i>et al.</i>	CR	2019	UK	1
39.	Thakur <i>et al.</i>	CR	2019	India	1
40.	Abdalla <i>et al.</i>	CR	2020	UK	1
41.	Andinata <i>et al.</i>	CR	2020	Indonesia	1
42.	Dhia <i>et al.</i>	CR	2020	Tunisia	1
43.	Nwabuoku <i>et al.</i>	CR	2020	Nigeria	1
44.	Jung <i>et al.</i>	CR	2021	South Korea	1
45.	Almeida <i>et al.</i>	CR	2023	Portugal	1
46.	Gholami <i>et al.</i>	CR	2023	Iran	1
47.	Mansikka <i>et al.</i>	CR	2023	Finland	1
48.	Peron <i>et al.</i>	CR	2023	Brazil	1

CR: Case report, CS: Case series, OR: Original research, RA: Retrospective analysis, UK: United Kingdom, USA: United States of America

The patients' mean age was 56.7 years (range 36-76). 66% patients had a previous history of BC, whereas 29%

Table 2: Clinical data of patients with Breast cancer metastasizing to Salivary glands (March 1975–March 2023)

P. No.	Age (years)	PHOBC	Salivary gland involved (Side)	Clinical features	Initial site of metastasis?	Time of diagnosis of metastasis	Any other site of metastasis?	Final diagnosis of BC	Side of BC
1.	NA	NA	SMG (NA)	Swelling	NA	-	NA	NA	NA
2.	NA	Y	SMG (NA)	Swelling	N	19 Yr.	NA	NA	NA
3.	62	N	P (L)	Swelling	Y	-	NA	ILC	L
4.	61	N	P (L)	Swelling	Y	-	NA	IDC	L
5.	74	N	P (L)	FNP	Y	-	NA	NA	L
6.	68	Y	SMG (NA)	Swelling	N	4 Yr.	NA	NA	NA
7.	41	Y	P (L)	FNP	N	10 Yr.	NA	IDC	R
8.	65	Y	P (L)	Swelling	N	NA	NA	IDC	R
9.	57	NA	P (L)	Pain	NA	-	NA	IDC	R
10.	NA	Y	SMG (NA)	Soft painless swelling	N	2 Yr.	N	IDC	NA
11.	42	N	P (BL)	Painless, elastic swelling	Y	-	N	IDC	L
12.	52	N	P (R)	Mass	Y	-	N	IDC	R
13.	57	N	P (L)	Mass	Y	-	N	IDC	L
14.	NA	N	P (R)	Mass	Y	-	NA	NA	NA
15.	71	NA	P (R)	FNP	NA	-	NA	IDC	R
16.	NA	NA	SMG (L)	Painless mass	NA	-	NA	NA	NA
17.	66	Y	P (L)	FNP	N	15 Yr.	NA	IDC	R
18.	58	N	P (R)	Swelling	Y	-	NA	IDC	R
19.	40	Y	P (R)	Mass	N	NA	NA	MPT	L
20.	NA	NA	P (NA)	Swelling	NA	-	NA	IDC	NA
21.	NA	NA	P (NA)	Swelling	NA	-	NA	IDC	NA
22.	61	Y	P (L)	Swelling	N	5 Yr.	NA	IDC	L
23.	52	Y	P (L)	Mass	N	2 Yr.	NA	IDC	L
24.	42	Y	P (L)	Swelling	N	1 Yr.	NA	IDC	R
25.	63	N	P (R)	Swelling	Y	-	NA	undifferentiated	R
26.	65	Y	P (L)	Swelling	N	11 Mo	NA	ILC	L
27.	70	Y	P (L)	Swelling, pain	N	1.5 Yr.	Thyroid, bone, Liver	IDC	L
28.	50	Y	SMG (R)	NA	N	9 Yr.	NA	IDC	R
29.	74	Y	P (R)	FNP	N	4 Yr.	Bone	ILC	L
30.	43	N	P (L)	NA	Y	-	Bone, Liver	IDC	L
31.	61	N	P (R)	Swelling	Y	-	Axilla, left surrenal gland	IDC	R
32.	76	Y	P (R)	NA	N	25 Yr.	N	IDC	R
33.	60	Y	P (R)	Hard swelling	N	7 Yr.	N	IDC, mucinous	R
34.	61	Y	P ®	Swelling	N	1 Yr.	N	IDC	R
35.	65	Y	P (R)	Swelling	N	6 Yr.	NA	IDC	R
36.	48	N	P (R)	Swelling	Y	-	N	IDC	R
37.	43	N	P (L)	Painless swelling	Y	--	N	IDC	R
38.	NA	Y	P (NA)	NA	N	11 Mo	NA	IDC	R
39.	71	Y	P (L)	Painful mass	N	26 Yr.	N	IDC	R
40.	48	Y	P (R)	Swelling	N	11 Yr.	N	IDC	L
41.	36	Y	P (R)	FNP	N	11 Mo	LN, Bone, Lung, Right breast	IDC	R
42.	60	Y	P (R)	Swelling	N	9 Mo	N	IDC	R
43.	54	Y	P (R)	Swelling, FNP	Y	11 Mo	Bone, Sacrum, Lung	IDC	R
44.	54	N	P (L)	Swelling	Y	-	Bone	IDC	L
45.	59	Y	P (L)	Swelling	N	8 Yr.	N	IDC	R
46.	55	Y	P (L)	Swelling, Bell's palsy	N	11 Mo	N	IDC	L
47.	60	Y	P (R)	Lump	N	20 Yr.	Vert	IDC	L
48.	39	Y	P (L)	Lump	N	3.5 Yr.	Bone	IDC	L

Contd...

Table 2: Contd...

P. No.	Age (years)	PHOBC	Salivary gland involved (Side)	Clinical features	Initial site of metastasis?	Time of diagnosis of metastasis	Any other site of metastasis?	Final diagnosis of BC	Side of BC
49.	50	Y	P (BL)	Swelling	N	9 Yr.	Bone, Brain, Skin	IDC	L
50.	62	Y	P (L)	Lump	N	1 Wk.	N	Poorly diff	R
51.	59	Y	P (L)	Swelling	N	6 Yr.	LN, Lung, Neck	IDC	L
52.	50	Y	SLG	Swelling	N	3 Yr.	Lung, Liver, Bone	IDC	L
53.	40	Y	SMG (L)	Swelling	N	10 Yr.	N	ILC	R
54.	69	N	P (L)	Swelling	Y	-	Bone	ILC	R
55.	50	N	P (L)	Swelling	Y	-	Axillary LN	IDC	L

BC: Breast cancer, BL: Bilateral, FNP: Facial nerve palsy, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, L: Left, LN: Lymph node, M: Male, Mo: Months, MPT: Malignant Phylloides Tumor N: No, NA: Not available, P: Parotid, PHO: Previous history of, R: Right, SLG: Sublingual Gland, SMG: Submandibular Gland, Y: Yes, Yr.: Years

Table 3: Data describing treatment and prognosis of patients with Breast cancer metastasizing to Salivary glands (March 1975–March 2023)

Pt. No.	Treatment given	Prognosis	Survival time from diagnosis of metastasis to death (Months)
1.	NA	NA	NA
2.	NA	NA	NA
3.	R	NA	NA
4.	Combined (P, C)	NA	NA
5.	Combined (C, R)	NA	NA
6.	NA	NA	NA
7.	R	NA	NA
8.	Combined (C, R)	NA	NA
9.	p	NA	NA
10.	NA	NA	NA
11.	Combined (C, R, M)	D	2
12.	NA	D	15
13.	NA	Fav	-
14.	NA	NA	NA
15.	P	NA	NA
16.	NA	NA	NA
17.	P	D	5
18.	Combined (P, C, R)	D	5
19.	P	Fav	-
20.	Combined	NA	NA
21.	Combined	NA	NA
22.	Combined (P, C, R)	Fav	-
23.	Combined (P, C, R)	NA	-
24.	RBP	NA	-
25.	H	UFU	-
26.	Combined (C, P)	D	NA
27.	Combined (P, R)	LFU	-
28.	S	Fav	-
29.	P	NA	NA
30.	P	D	8
31.	Combined (P, R)	Fav	-
32.	H	NA	NA
33.	Combined (C, R, H)	NA	NA
34.	Combined (P, R, H)	Fav	-
35.	Combined (P, R)	NA	NA
36.	Combined (P, C, R, M)	NA	NA
37.	Combined (P, C, R, M)	NA	NA
38.	P	NA	NA
39.	H	Fav	-

Contd...

Table 3: Contd...

Pt. No.	Treatment given	Prognosis	Survival time from diagnosis of metastasis to death (Months)
40.	Combined (C, R)	Fav	-
41.	H	Fav	-
42.	Combined (C, R)	NA	NA
43.	C	Fav	-
44.	Combined (C, H)	Fav	-
45.	Combined (P, RND)	Fav	-
46.	Combined (P, C)	NA	NA
47.	P	Fav	-
48.	Combined (P, C, R)	NA	NA
49.	Combined (Palliative, C)	D	12
50.	Planned	LFU	-
51.	C	D	2
52.	Combined (C, R, I, RND)	UFU	-
53.	NA	NA	NA
54.	Combined (P, C, H)	Fav	-
55.	Combined (P, H)	Fav	-

C: Chemotherapy, D: Death, Fav: Favourable, H: Hormonal, LFU: Lost to follow up, NA: Not available: Pt No.: Patient's number, P: Parotidectomy, R: Radiotherapy, RBP: Refused by patient, RND: Radical neck dissection, S: Surgery, TGO: Treatment going on, Tt: Treatment, UFU: Under follow up

had none. The parotid gland was the most predominant site of metastasis (85.4%) followed by the submandibular gland (12.7%). In both glands, the left side was affected more than the right. In 31% of cases, SG was the initial site of metastasis, whereas in 58.2% cases, it was detected later with an average time of 1 week to 26 years. In 29% cases, SG was the only site of metastasis, whereas in 25.4% cases, it involved other body sites also. In 51% cases, there was an ipsilateral spread, and in 27.3% cases, it was contralateral. The most common type of BC diagnosed was invasive ductal carcinoma (IDC) followed by invasive lobular carcinoma (ILC). Major therapeutic aids included were combined therapies (49%). 14.5% of patients died with a mean survival rate of 7 months. 27.3% had a favorable prognosis [Table 4].

DISCUSSION

BC is the first and second leading cause of cancer-related death in developing and developed countries, respectively. In the past few years, the cases of BC have rapidly increased in developed countries, mostly Australia, Western Europe, and Northern America.^[2] In the current research, the maximum number of cases was from the UK (23.6%) followed by India (11%) and USA (7.3%). Other regions involved a few cases [Table 4].

BC occurs predominantly during the 5th-6th decade. Metastatic involvement of the SG in BC patients has been reported at different ages (3rd-7th decade)^[44]. In the current study also, the age ranged between 3rd and 7th decade. Multiple underlying Factors favor the development of BC, which include obesity, hormonal and reproductive risk factors, alcohol, drug usage,

malnutrition, genetic mutations, etc.^[2] In the current research, we could not document any associated risk factors reported by the patients. Only a few had a history of obesity and family history of BC.

Distant spread of BC most often occurs in the lungs, bones, liver, and brain. SG is the rarest site. And if this occurs, the parotid is the most affected gland. According to the current research, we could find only 55 such cases reported in the last 48 Years (March 1975–March 2023). Parotid was the most common gland affected (85.4%), whereas 12.7% of metastatic sites were in submandibular gland. Only one case involved the sublingual gland. The left side of both glands was more predominantly affected than the right. In 51% cases, ipsilateral spread was there and in 27.3% cases, contralateral spread was there.

The route of secondary metastasis to the SG may be either lymphatic, homogeneous, or direct invasion.^[3] Abundant lymphatic tissue in the parotid leads to lymphatic spread. However, metastatic BC spreads to the SG predominantly following the hematogenous route. One of the proposed pathways is via Batson's valve plexus system.^[36]

Oral metastatic tumors are of high clinical importance because they may be the only symptom of an undiagnosed underlying malignancy or the first sign of metastasis. Both synchronous and metachronous involvement of SG has been reported in the literature. In the current study, SG was the initial site of metastasis in 31% of cases, whereas, in 58.2% of cases, metastasis was detected late after the diagnosis and treatment of BC, with a range of 1 week to 26 yrs.

Table 4: Summary of results documented from literature research describing the characteristics of patients with Breast cancer metastasizing to Salivary glands (March 1975–March 2023)

Feature	Number
Total number of papers published	48 <ul style="list-style-type: none"> Case reports-43 Retrospective analysis -3 Original research-2
Total number of patients	55
World-wide distribution of cases	<ul style="list-style-type: none"> UK-13 (23.6%) India-6 (11%) USA-4 (7.27%) Israel=Poland=Spain=Turkey-3 (5.4%) Germany=Iran=Italy=Tunesia-2 (3.6%) Africa=Brazil=China=Finland=Japan=Ireland=Indonesia=Kuwait=Nigeria=Portugal=South Korea- 1 (1.8%)
Average age of patients (Mean, Range)	• 56.68 (36-76)
Previous history of BC	<ul style="list-style-type: none"> Y-33 (66%) N -16 (29%) NA-6 (11%)
SG involved in metastasis	<ul style="list-style-type: none"> Parotid -47 (85.4%) <ul style="list-style-type: none"> (R- 18 (38.3%), L-24 (51.1%), BL-2 (4.25%), SNA-3 (5.4%) SMG - 7 (12.7%) <ul style="list-style-type: none"> (L-2 (28.6%), R-1 (14.3%), SNA-4 (57.1%) SLG-1 (1.8%)
SG as the initial site of metastasis	<ul style="list-style-type: none"> Y - 17 (31%) N - 32 (58.2%) NA-6 (11%)
Any other site of metastasis	<ul style="list-style-type: none"> Y-14 (25.45%) N- 16 (29.1%) NA- 25 (45.4%)
Clinical features	<ul style="list-style-type: none"> Swelling-34 (75.5%) FNP-8 (14.5%) Mass-7 (12.7%) Lump-3 (5.4%) NA-3 (6.4%)
Average mean time of detection of SG metastasis	• 1 week to 26 Years
Final diagnosis of metastatic BC	<ul style="list-style-type: none"> IDC-41 (74.5%) ILC-5 (9%) MPT-1 (1.8%) Undifferentiated-1 (1.8%) Poorly differentiated -1 (1.8%) NA-6 (11%)
Side of BC spread	<ul style="list-style-type: none"> I-28 (51%) C-15 (27.3%) BL-2 (3.6%) NA-10 (18.2%)
Treatment aids	<ul style="list-style-type: none"> Combined therapy-27 (49%) Parotidectomy-8 (14.5%) Hormonal- 4 (7.3%) Chemotherapy-2 (3.6%) Radiotherapy-2 (3.6%) Surgery -1 (1.8%) RBP-1 (1.8%) NA-8 (14.5%) NG-1 (1.8%)
Overall Prognosis	<ul style="list-style-type: none"> Deaths- 8 (14.5%) Favourable-15 (27.3%) NA- 28 (51%)

Contd...

Table 4: Contd...

Feature	Number
	<ul style="list-style-type: none"> LFU- 2 (3.6%) UFU- 2 (3.6%)
Average mean survival time from diagnosis of SGT to death	<ul style="list-style-type: none"> 7 Months (2-15 Months)

BC: Breast cancer, BL: Bilateral, C: Contralateral, F: Female, FNP: Facial nerve paralysis, I: Ipsilateral, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, L: Left, LFU: Lost to follow up, M: Male, Mon: Months, MPT: Malignant phylloid tumor, N: No, NA: Not available, NG: Not given, R: Right, RBP: Refused by patient, SG: Salivary gland, SGT: Salivary gland tumor, Tt: treatment, UFU: Under follow up, UK: United Kingdom, USA: United States of America, Y: Yes, Yr.: years

Clinically, metastatic BC to SG is characterized by periauricular mass, swelling, and lump, sometimes with signs of peripheral facial nerve palsy.^[44] These metastatic lesions often become difficult to diagnose because their variable appearance bear close resemblance to primary neoplastic or non-neoplastic SG lesions. In the present research, swelling was the most predominant clinical feature observed (75.5%) and in 14.5% cases, there was involvement of facial nerve palsy.

To exclude the primary malignancies of SG, a history of primary BC in the patient could be a guiding tool for detecting the secondary deposits. Before the metastatic spread to the oral cavity, the majority of patients are often aware of their primary tumors. However, patients may manifest the symptoms even after a long time of primary tumor detection. In the current research, 66% of patients had a previous history of primary BC, whereas 29% of patients did not reveal such history.

SGTs need a proper evaluation for diagnosing the type of malignancy, whether it is benign or malignant. Ultrasonic examination is the prime choice in the diagnosis of SG swellings. Fine needle aspiration biopsy is another diagnostic aid used for these lesions, but its diagnostic value is controversial, due to the high false-negative rate. A biopsy is recommended for the histopathological examination for providing a conclusive diagnosis of the type of metastatic lesion. However, it might be difficult to make an exact diagnosis because of varied histological appearance, particularly when the major focus of the primary site is unknown. Histopathologically, BC has been divided into various subgroups.^[57] IDC is the most predominant type and has been discovered to be the most prevalent metastasizing to the SG. Histopathologically, many of SG primary malignancies such as salivary duct carcinoma resemble the metastatic BC including immunoprofiles which make the differentiation difficult. Despite similarities, there are some characteristics that can be valuable in making an accurate diagnosis. In metastatic ductal carcinoma, residual normal parotid acini can be seen between the neoplastic glands,

whereas salivary duct carcinoma is expansile, leaving no or very rare normal gland elements between its neoplastic cells. In addition, metastasis from BC lacks the pattern of intraductal cribriform carcinoma that is characteristic of primitive salivary duct carcinoma of the parotid gland. Some studies have reported immunohistochemical staining to have limitations in distinguishing between primary SDC of the parotid gland and IDC from BC. However, others claim that immunohistochemical staining can provide valuable information, and the absence of expression of estrogen and progesterone receptors favors the diagnosis of a salivary duct carcinoma.^[36]

Imaging techniques such as computerized tomography scans and magnetic resonance imaging can help in the assessment for possible extension or invasion. Positron emission tomography is useful in detecting distant organ metastasis. Although BC entails multiorgan distant metastases, SG might occasionally be the only site of metastasis many times. 16 out of 55 instances in this study had SG as the only location of BC metastasis, whereas 14 had metastasis to other regions as well such as lungs, brain, liver, and vertebrae.

The treatment of choice for primary BC ranges from mastectomy to chemotherapy, radiotherapy, and hormonal therapy or even the palliative treatment. Management for SG metastatic disease includes a combination of surgical removal of solitary tumors, chemotherapy, radiotherapy, endocrine therapy, and targeted therapy. For single parotid metastasis, parotidectomy (total or superficial) with negative margins (preferably with preservation of facial nerve) and postoperative radiotherapy to obtain local tumor control and to exclude a primary parotid tumor. The most commonly used therapeutic aids in this study were combined therapy (49%). In 14.5% cases, parotidectomy (either superficial, deep, partial, or total depending on the site) with preservation of facial nerve was performed. Other therapies used were chemotherapy, radiotherapy, and hormonal. Despite the proposed treatments, patients with metastatic involvement of the parotid gland have poor prognosis, with the 5-year survival rate reported to be 10%. According to the current study, only 14.5% of individuals died with an average survival time of 7 months. 27.3% of patients had a good prognosis with no signs of recurrence. In 2 patients, treatment is going on. Two cases are under follow-up.

Limitations of the current study

One of the limitations of current research was small sample size. Most of studies included were case reports and case series. And in many of the included studies, individual data of patients were not available.

CONCLUSIONS

During the last 48 years (March 1975–March 2023), we found only 55 cases of BC metastasizing to SG. This signifies a rare occurrence of SG metastasis from BC. 14.5% of patients died with a mean survival rate of 7 months. Parotid was the most affected gland followed by SMG. Because of their resemblance to primary neoplastic and non-neoplastic SG lesions, metastatic lesions go unnoticed the majority of the time. Their diagnosis is a challenging task for 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.

Abbreviations

BC: Breast cancer, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, NA: Not available, SG: Salivary glands, SGT: Salivary gland tumors.

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Conflicts of interest

There are no conflicts of interest.

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