Review Article

Metastasis to jaw bones from renal cell carcinoma as the sole primary source: Systematic review

ABSTRACT

Renal cell carcinoma (RCC) has been known for its high propensity of metastasis to unusual locations, and jaw bones (JBs) are one among those sites. The literature has reported several studies analyzing metastatic tumors to the oral region, but very little research work has been published to date to analyze solely JB metastasis (JBM) via RCC. The goal of this study was to examine the published cases of metastasis to JBs from RCC as the sole primary source till date. An electronic search of the published literature was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines without publication year limitation in PubMed or MEDLINE, Scopus, Google Scholar, Web of Science, ScienceDirect, Embase, and Research Gate Databases, using MeSH keywords, such as ('Renal cancer', OR 'Renal carcinoma' OR 'Renal cell cancer' OR 'Renal cell carcinoma'), AND ('Metastasis' OR 'Metastases') And ('Jaw' OR 'Maxilla' OR 'Mandible') And ('Temporomandibular joint' OR 'Condyle' OR ' Ramus'). We also searched all related journals manually. The reference list of all articles was also checked. Our research revealed a total of 56 relevant papers with 66 patients. The papers included were from 1939 to 2022. The mandible was the most predominant jaw affected than the maxilla. 19.7% of patients died with a mean survival time of 8.5 months. From the current research, it can be concluded that metastasis to JBs from RCC is a rare occurrence. A careful evaluation of these cases is needed to raise awareness of these lesions and gain a better understanding of their characteristics.

Keywords: Jawbones, metastasis, renal cell carcinoma

Sonia Gupta, Aruna Vanka[1], Shreya Gupta[2], Harnisha Vipulkumar Prajapati[3], Ruchira Shreevats[4], Manasi Pangarkar[5], Mrunali Desai[6], Arun Raj[7], Fatema Matcheswala[8]

Department of Oral Pathology, Yamuna Institute of Dental Sciences & Research, Gadholi, Yamunanagar, Haryana, [1]Consultant Periodontist, Devi Dental Clinic, Hyderabad, Telangana, [2]Department of Pedodontics, Sudha Rustagi College of Dental Sciences, Faridabad, Haryana, [3]Private Practitioner, Bhavya Dental Clinic and Implant Centre, Palanpur, Gujarat, [4]Consultant Orthodontist, Primadent Dental Centre, Bengaluru, Karnataka, [5]Private Practitioner, The Tooth Place Dental Clinic, Mumbai, Maharashtra, [6]Department of Oral Pathology and Microbiology and Forensic Odontology, K.M Shah Dental College and Hospital, Vadodara, Gujarat, India, [7]DMD, Perfect Smile Richmond, United Kingdom, [8]Certified Dental Assistant, Ladner Village Dental, Vancouver, BC, Canada

Address for correspondence: Dr. Sonia Gupta, #95/3, Adarsh Nagar, Dera Bassi, Mohali, Punjab - 140 507, India.
E-mail: Sonia.4840@gmail.com

Received: 24 May 2023, **Revised:** 08 August 2023, **Accepted:** 19 October 2023, **Published:** 16 November 2024

INTRODUCTION

Renal cell carcinoma (RCC) is the seventh most common histological type of cancer in the Western world, originating from the proximal renal tubular epithelium. Worldwide, 403,000 new cases of RCC and 175,000 deaths due to this malignancy were recorded in 2018.[1] In India, the incidence of RCC among males is about 2/100000 population and among females is about 1/100000 population.[2] One of the unique features of RCC is its long-term asymptomatic clinical behavior and high risk of distant organ metastasis in the advanced stages. Only in 10% of patients, a "classic triad" of symptoms, that is, hematuria, flank pain, and palpable masses, has been noticed.[3] Approximately 18% of patients with RCC present with metastasis at the time of diagnosis, and in >50% of cases, metastasis is detected during the follow-up period after nephrectomy.[4] The most common organs involved in distant metastasis of RCC are the lungs, bones, lymph nodes, liver, adrenal glands, and brain.[5] Tumor

Access this article online	
Website: www.njms.in	Quick Response Code
DOI: 10.4103/njms.njms_91_23	

How to cite this article: Gupta S, Vanka A, Gupta S, Prajapati HV, Shreevats R, Pangarkar M, *et al.* Metastasis to jaw bones from renal cell carcinoma as the sole primary source: Systematic review. Natl J Maxillofac Surg 2024;15:367-78.

metastasis to the oral cavity is uncommon, comprising only 1% of all oral malignant tumors. After lung and breast carcinoma, RCC is the third most common tumor that metastasizes to the head and neck.[6] Metastasis to the orofacial region has been well documented in the skin, subcutaneous tissue, parotids, and paranasal sinuses. The involvement of the jaw bones (JBs) is extremely rare with only a few reports. The literature has reported several studies analyzing metastatic tumors to the oral region,[6-8] but very little research work has been published to date to analyze solely JB metastasis (JBM) via RCC. Thus, this review was conducted to examine the published cases of JBM from RCC in the literature from 1939 to 2022 and to learn about their characteristics.

MATERIALS AND METHODS

The current research was conducted following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Owing to the 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 RCC metastasizing to JB have been documented in the literature, and what is the prognosis of these metastatic lesions?"

Pop (population): Patients with RCC

Co (condition): JBM

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 or MEDLINE, Scopus, Google Scholar, Web of Science, ScienceDirect, Embase, and Research Gate databases, using MeSH keywords, such as ('Renal cancer', OR 'Renal carcinoma' OR 'Renal cell cancer' OR 'Renal cell carcinoma'), AND ('Metastasis' OR 'Metastases') And ('Jaw' OR 'Maxilla' OR 'Mandible' And ('Temporomandibular joint' OR 'Condyle' OR ' Ramus'). 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 and AV) independently and duplicates were removed. Then, the other four authors (SG, HVP, RS, and MP) reviewed the selected abstracts of all the reports independently. The reviewers were calibrated based on their assessment of their titles, and abstracts of the first 50 references were retrieved. The kappa value of agreement between reviewers was 0.82. If the title or abstracts met the eligibility rule, they were included in the study. In the final stage, the text of selected studies was screened by the remaining three authors (MD, AR, and FM) 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 JBM via RCC. The papers included were from 1939 to 2022.
- Type of studies: Case reports, case series, and retrospective analysis.
- Cases were selected beyond the restriction of limitations on parameters, such as age, gender, ethnicity, or socioeconomic status.
- Articles published in any language were included.

Exclusion criteria

- Cases with no definite diagnosis of JBM via RCC were excluded.
- Publications reporting the JBM from any primary site other than the kidney were excluded.
- Cases with RCC metastasis to oral soft tissues and paranasal sinuses were not included.
- Studies that did not provide individual patient data were excluded.
- Editorials, conference abstracts, hypothesis papers, Web news, media reports, and animal studies.

Outcome measures

Primary outcome measures

To evaluate the number of cases of JBM via RCC reported in the literature and to determine their prognosis.

Secondary outcome measures

To evaluate other factors, such as worldwide distribution of cases, patient's demographic details, associated risk factors, predominant site of JBM, clinical features of these metastatic lesions, the most prevalent type of metastatic RCC, and type of therapies used.

Risk of bias assessment

Most of the studies included in this review were case reports and case series. The risk of bias was appraised following CARE and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklists.[9,10] In several papers,

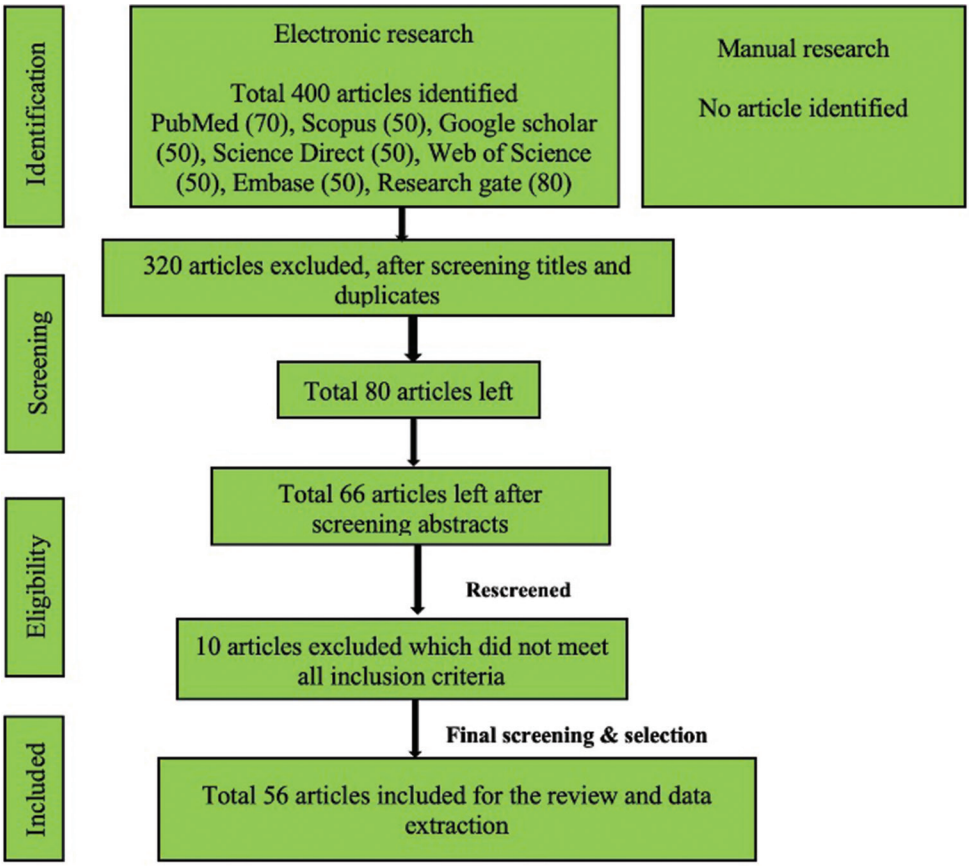

Figure 1: PRISMA flowchart showing search strategy

there was missing information regarding many parameters used for data extraction. We tried reaching the authors of those cases to clarify this bias; however, we were unable to recover the missing information.

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

Our research strategy revealed a total of 56 relevant papers (a few references).[11-37] The papers included were from 1939 to 2022. A total of 66 patients included 36 males and 17 females with a male-to-female ratio of 2.1:1. The maximum number of cases were from the USA (n = 18), followed by Japan (n = 10), the UK (n = 6), and India (n = 5). The patients' mean age was 54.1 years (range 1–89). The mean age was 53.5 years in males and 52.3 years in females. 15.2% of patients had a previous history of RCC, while 31.8% had none. The mandible was the most predominant jaw involved (74.2%) than the maxilla (21.2%). Only two cases involved temporomandibular joint (TMJ). In both jaws, the left side is affected more than the right. Most of the cases did not reveal the side of involvement in both jaws. In 31.8% of cases, JB was the initial site of metastasis, and in 11.6% of cases, JB was the only site of metastasis. The most common type of RCC diagnosed was clear cell carcinoma (CCC). Major therapeutic aids included were combined therapies (27.7%), followed by surgery (6.1%) [Table 4]. 19.7% of patients died with a mean survival rate of 8.5 months [Table 4].

DISCUSSION

RCC is one of the lethal neoplasms, leading to approximately 2% of global cancer diagnosis and deaths, projecting to increase in burden worldwide. In the past few years, the cases of RCC have rapidly developed in developed countries, mostly the USA.[36] In the current research also, the maximum number of cases was from the USA (n = 18), followed by Japan (n = 10), UK (n = 6), and India (n = 5). Other regions involved a few cases [Table 4].

Table 1: Details of publications included in the current review (1939-2022)[11-37]

S. no.	Authors	Year	Country	Type of study	Total no. of patients
1.	Vogt	1939	Germany	CR	1
2.	Stewart and Bruce	1953	USA	CR	1
3.	Nesbitt	1959	USA	CR	1
4.	Shimosato *et al*.	1959	Japan	CR	1
5.	Mallett	1961	USA	CR	1
6.	Meyer and Shklar	1965	USA	RA	4
7.	Doyle and Goldman	1966	USA	CR	1
8.	Myres	1967	USA	CR	1
9.	Maki *et al*.	1970	Japan	CR	1
10.	Boles *et al*.	1971	USA	CR	1
11.	Dehner	1973	USA	RA	1
12.	Colonius *et al*.	1975	Finland	CR	1
13.	Milobasky *et al*.	1975	USA	CR	1
14.	Tani *et al*.	1976	Japan	CR	1
15.	Nagayama and Oka	1979	Japan	CR	1
16.	Stypulkowska *et al*.	1979	USA	RA	2
17.	Quinn *et al*.	1981	USA	CR	1
18.	Bucin *et al*.	1982	Sweden	CR	1
19.	Nishimura *et al*.	1982	Japan	RA	3
20.	Sidhu *et al*.	1982	India	CR	1
21.	Favia *et al*.	1986	Japan	CR	1
22.	Pick *et al*.	1986	USA	CR	1
23.	Florine *et al*.	1988	USA	CR	1
24.	Zachariadies *et al*.	1989	Greece	CS	1
25.	Jones *et al*.	1990	UK	CR	2
26.	Ord *et al*.	1990	UK	CR	2
27.	Sánchez Aniceto *et al*.	1990	Spain	CR	1
28.	Lee *et al*.	1998	UK	CR	1
29.	Pruckmayer *et al*.	1998	Austria	CS	1
30.	Guyot *et al*.	1999	France	CR	1
31.	Honig	2000	Germany	CR	1
32.	Toranzo-Fernandez *et al*.	2000	Mexico	CR	1
33.	Shetty *et al*.	2001	India	CR	1
34.	Zakaria *et al*.	2004	Malaysia	CR	1
35.	Sastre *et al*.	2005	Spain	CR	1
36.	Heinroth *et al*.	2006	Germany	CR	1
37.	Jia *et al*.	2006	China	CR	1
38.	Muttagi *et al*.	2011	India	RA	1
39.	Kelleys *et al*.	2012	Turkey	CR	1
40.	Murakami *et al*.	2012	Japan	CR	1
41.	Ahmadania *et al*.	2013	Iran	CR	1
42.	Jallu *et al*.	2013	India	CR	1
43.	Zhang *et al*.	2014	China	CR	2
44.	Liuzzi *et al*.	2015	Greece	CR	1
45.	Shah *et al*.	2016	India	CR	1
46.	Gooran *et al*.	2017	Iran	CR	1
47.	Laeider *et al*.	2017	Germany	CR	1
48.	Derakhshan *et al*.	2018	Iran	CR	2
49.	Ardhaoui *et al*.	2019	Morocco	CR	1
50.	Netto *et al*.	2019	Brazil	CR	1
51.	E Bassey *et al*.	2020	Nigeria	CR	1
52.	Ludwig *et al*.	2020	USA	CR	1
53.	Nishi *et al*.	2020	Japan	CR	1
54.	Zhang *et al*.	2020	UK	CR	1
55.	Paraskevopoulos *et al*.	2021	Greece	RA	1
56.	Jung *et al*.	2022	Korea	CR	1

Contd...

Table 1: Contd...

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

RCC occurs predominantly during the 5th–6th decade exhibiting a male predilection with a male-to-female ratio of 1.5:1. In the current study also, there was a male predominance, with M: F =2.1:1. However, the age ranged between first and eighth decades.[4]

Multiple risk factors favor the development of RCC, which include smoking, tobacco chewing, alcohol, obesity, and hypertension.[4] Smokers are known to exhibit more risk of RCC than nonsmokers.[37] Patients with underlying comorbidities are at a higher risk of developing cancer owing to a lack of immunity.[4] In this research, we found that 15.4% of cases had a history of associated risk factors and comorbidities, the most common of which were hypertension and associated renal diseases. Very few patients reported a history of smoking and tobacco habit [Table 4].

Distant spread of RCC most often occurs in the lungs, bones, lymph nodes, liver, adrenal glands, brain, and skin. JB is the uncommon site of distant metastasis from RCC. If this occurs, the mandible is the predominant jaw involved than the maxilla. According to the current research, the first case of JBM from RCC was reported in 1939 by Vogt *et al*.[11] Since then, we have found only 65 such cases reported in the last 83 years (1939–2022). The mandible was the most common site of JBM than the maxilla with a predominance of the posterior and left side involvement in both jaws.

Pathogenic mechanisms of JBM are not completely understood. It is via lymphatic or hematogenous channels.[38] One of the proposed pathways is the "Batson's plexus," a valveless prevertebral venous plexus network that involves retrograde tumor cell movement from the lungs to the face.[39] Because the JB does not have lymphatic capillaries, hematogenous metastasis is the most prevalent route here. A rich capillary network acts as the milieu for the localization of tumor cells. Metastatic foci are more common in red bone marrow than fatty marrow, which allows for greater trapping of metastatic cells due to the slow regulation of blood flow control. JBM is more common in the mandible (posterior area notably the body (premolar–molar region), angle, and ascending ramus) than in the maxilla, owing to the existence

Table 2: Clinical data of patients with jaw bone metastasis from renal cancer as the sole primary source (1939–2022)

Pt. NO.	Age	Sex	PHORCC	Risk factors	Site of jaw	C/C	C/F	R/F	Initial site?	TOM	Other sites	Final diagnosis
1	63	M	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
2	70	M	NA	NA	Mand	NA	NA	NA	NA	NA	Lung, brain, bone	CCC
3	4	M	NA	NA	Mand	NA	NA	NA	NA	NA	Lung, bone	CCC
4	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	Lung, bone	CCC
5	62	F	NA	NA	Mand	NA	NA	NA	NA	NA	SMG	CCC
6	57	M	NA	NA	Mand	NA	NA	NA	NA	NA	Bone	CCC
7	48	M	NA	NA	Max	NA	NA	NA	NA	NA	Lung	CCC
8	73	F	NA	NA	Mand	NA	NA	NA	NA	NA	Bone	CCC
9	43	M	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
10	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
11	2 Y. ¾ Mon	F	Y	NA	Mand/L/ Post	Rapidly growing mass	Growth extending molar pushing tooth out of occlusion	Tooth out of occlusion	N	3	Tibia	CCC
12	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	Adr	CCC
13	53	M	NA	NA	Mand	NA	NA	NA	NA	NA	N	CCC
14	1	M	N	NA	Mand	Rapidly growing mass	NA	OL	Y	-	NA	CCC
15	81	F	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
16	66	F	NA	NA	Max	NA	NA	NA	NA	NA	NA	CCC
17	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
18	61	M	N	HT, MI	Mand, R, Post	Swollen right cheek	6 X 4 X 4 cm diffuse swelling	NA	Y	-	Adr	CCC
19	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	Lung	CCC
20	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	Bone, liver	CCC
21	52	M	NA	NA	Mand, L	Swelling in lower back jaw	Pulsatile swelling	NA	NA	NA	Lung	CCC
22	67	M	Y	NA	Mand, Ant	Painful swelling	Tender mass	OL	N	84	NA	CCC
23	61	F	NA	NA	Mand	Swelling, pain, paraesthesia, tooth mobility	Tender mass	OL	NA	NA	NA	CCC
24	61	M	NA	NA	Mand	Swelling, pain, paraesthesia, tooth mobility	Tender swelling, loose teeth, loose teeth	OL	NA	NA	NA	CCC
25	36	F	NA	NA	Mand	Swelling, pain, paraesthesia, tooth mobility	Tender swelling, lose teeth	OL	NA	NA	NA	CCC
26	NA	NA	N	NA	Mand	Vascular growth	Erythematous swelling	NA	Y	-	NA	CCC
27	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
28	71	M	N	NA	Mand	Painless swelling	Nontender swelling	NA	Y	-	Bone	CCC
29	NA	M	Y	NA	Mand	NA	NA	NA	N	18	Bone	CCS
30	78	M	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
31	52	F	N	NA	Mand	Vascular swelling	Erythematous mass	NA	Y	-	Bone	CCC
32	62	F	N	NA	Mand	Vascular swelling	Erythematous mass	NA	Y	-	NA	CCC
33	NA	NA	NA	NA	Max	Vascular swelling	Erythematous mass	NA	NA	NA	NA	CCC
34	NA	NA	NA	NA	Max	Vascular swelling	Erythematous mass	NA	NA	NA	NA	CCC

Contd...

Table 2: Contd...

Pt. NO.	Age	Sex	PHORCC	Risk factors	Site of jaw	C/C	C/F	R/F	Initial site?	TOM	Other sites	Final diagnosis
35	62	F	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
36	76	M	NA	NA	Max	NA	NA	NA	NA	NA	Ureter, bone	CCC
37	NA	NA	N	NA	Mand	Painful swelling	Tender mass	OL	Y	-	MM	CCC
38	83	F	NA	NA	Mand	Vascular swelling	Erythematous mass	NA	NA	NA	NA	CCC
39	16	M	Y	HLD	Max	Painful swelling	Tender mass	NA	N	6	Lung	CCC
40	8 Y	M	N	Wilms tumor	Mand, L	Rapidly growing mass on left side of face for 3 Mon	Tender swelling	OL	Y	-	NA	CCS
41	62	M	NA	NA	Mand	Solitary lesion with hematuria	Painful swelling	NA	NA	NA	NA	CCC
42	58	M	NA	NA	Mand, R, Post	Swelling and difficulty in eating for 6 Mon	Tender swelling	CT: Bone resorption at right side	NA	NA	Scapula, lung, humerus	CCC
43	NA	NA	NA	NA	Mand	NA	NA	NA	NA	NA	NA	CCC
44	53	F	NA	NA	Max	Vascular mass	Erythematous swelling	NA	NA	NA	Pelvic	CCC
45	3Y	M	Y	NA	Mand, L	NA	NA	NA	N	9	NA	CCC
46	53	M	Y	NA	Max Alveolus	Rapidly growing mass	Ulceroproliferative growth	NA	N	38	Lung	CCC
47	59	F	Y	NA	Condyle, L	Swelling and trismus in the left TMJ for 3 Mon	Hard firm mass 2 x 2 cm	CT: Irregular mass destructing the bone	N	3 6	NA	CCC
48	76	M	N	HT, To, A	Mand, R, A	Hypothesia	Tenderness in the mental region	OPG: OLCT: OL	Y	-	MM	CCC
49	57	M	N	NA	Mand, R	Swelling for 2 wk	2 x 3 cm soft mass, mobile molars	OPG: OL	Y	-	N	CCC
50	68	M	N	N	Mand, L, Post	Rapidly growing swelling	5 x 5 cm, firm, fixed mass	OPG: OLCT: OL	Y	-	N	CCC
51	45	M	Y	N	Mand, R, A	Rapidly growing swelling	4.0×3.0×2.5 cm with a clear border	OPG: OLCT: OL	N	24	N	CCC
52	60	M	Y	N	Max, A, BL	Slowly growing mass for 20 days	6.0×4.0×3.0 cm, ulceroproliferative, erythematous mass	OPG: OLCT: OL	N	48	Lung	CCC
53	54	M	N	N	Mand, L, A	Slowly growing mass for 3 Mon	Ulcerative mass	CT: OL	Y	-	N	CCC
54	22	M	N	UTI, Trauma	Mand, R, A	Swelling of right lower face since 1 Mon	Asymmetric face, bony hard, tender swelling	OPG: OL	Y	-	Rib, vertebrae, sternum	CCC
55	74	M	N	S	Both	Swelling on right side of face	Large hypervascular mass	CT: OL	Y	-	N	CCC
56	72	NA	N	N	Mand	NA	NA	NA	Y	-	Frontal bone	Small cell carcinoma
57	54	M	N	RCT	Max, Ant	Painful swelling	Pain and swelling and pus discharge	CT: OL	Y	-	Lung, nasal cavity, MS	CCC
58	51	M	N	N	Max, L, Post	Painless large mass for 2 Mon	Painful swelling	NA	Y	-	Lung	CCC
59	45	F	N	UTI, hematuria	Mand, R	Swelling for 4 Mon	5 x 4 cm mass with bleeding	OPG: RO	Y	-	Liver, lung	CCC

Contd...

Table 2: Contd...

Pt. NO.	Age	Sex	PHORCC	Risk factors	Site of jaw	C/C	C/F	R/F	Initial site?	TOM	Other sites	Final diagnosis
60	68	M	NA	HT, Gastritis	Max, R, Post	Rapidly increasing mass on right side of face	Tender, firm, tumor-like lesion	CT: OL	NA	NA	NA	CCC
61	43	F	NA	NA	Max, L, Post	Periorbital mass	8 x 7 cm periorbital soft, immobile, nontender mass involving cheek	NA	NA	NA	NA	CCpapillary
62	78	M	NA	NA	Mand, R, Post	Painful enlarging mass	Firm mass with bleeding	NA	NA	NA	NA	CCC
63	89	M	Y	N	Max, L	Swelling on left face	Firm, tender mass	OPG: bone resorptionCT: bone and max sinus destructionMRI: mass extending in max bone and sinus	N	84	Lung	CCC
67	56	F	N	HT, S	Condyle, R	Slowly increasing swelling onright side of face for 3 Mon	Tender to palpate the external oblique ridge and adjacent teeth	OPG:Complete destruction of the right condyle, coronoid, and ramus with an irregular non-corticated extension of the lesion into the body of the mandibleCT: large enhancing soft tissue mass with a central area of necrosis measuring 57×53 mm	Y	-	N	CCC
65	72	M	N	N	Mand, L	Slowly growing mass	Tender swelling	NA	Y	-	NA	CCC
66	22	F	N	N	Mand, L, post	Tumor mass on left side of face	Tender, ulcerative, swelling, reduced MO	MRI: enhancement along the medial pterygoid muscle surface while perforating the lingual cortical bone	Y	-	N	CCC

A: alcohol, Adr: adrenals, Ant: anterior, BL: bilateral, CC: chief complaint, CCC: clear cell carcinoma, DM: diabetes mellitus, F: female, HLD: Hippu lauder diseases, HT: hypertension, L: left, LN: lymph node, M: male, Mand: mandible, Max: maxilla, MI: myocardial infarction, Mon: months, MRI: magnetic resonance imaging, MS: maxillary sinus, N: no, NA: not available, OL: osteolytic, OPG: orthopantomogram, PHORC: previous history of renal cancer, Post: posterior, R: right, RCC: renal cell carcinoma, RCT: root canal treatment, R/F: radiographic features, S: smoking, SCC: small cell carcinoma, SMG: submandibular gland, TMJ: temporomandibular joint, To: tobacco, TOM: time of metastasis, UTI: urinary tract infection, Y: yes, Yr: years

Table 3: Data describing treatment and prognosis of patients with jaw bone metastasis from renal cancer (1939 to 2022)

Pt. no.	Treatment given	Prognosis	Survival time from diagnosis of metastasis to death (in months)
1	NA	NA	NA
2	NA	NA	NA
3	NA	NA	NA
4	NA	NA	NA
5	NA	NA	NA
6	NA	NA	NA
7	NA	NA	NA
8	NA	NA	NA
9	NA	NA	NA
10	NA	NA	NA
11	C, S	NA	NA
12	NA	NA	NA
13	NA	NA	NA
14	C, R, S	D	NA
15	NA	NA	NA
16	NA	NA	NA
17	NA	NA	NA
18	VPD, BT, R	D	2
19	NA	D	NA
20	NA	D	NA
21	NA	NA	NA
22	NA	NA	NA
23	NA	NA	NA
24	NA	NA	NA
25	NA	NA	NA
26	NA	NA	NA
27	NA	NA	NA
28	NA	NA	NA
29	C	NA	NA
30	NA	NA	NA
31	NA	NA	NA
32	NA	NA	NA
33	NA	NA	NA
34	NA	NA	NA
35	NA	NA	NA
36	NA	NA	NA
37	S	D	NA
38	Embolization	NA	NA
39	NA	NA	NA
40	NA	NA	NA
41	NA	NA	NA
42	PR	NA	NA
43	NA	NA	NA
44	S, C	NA	NA
45	S, C	NA	NA
46	S, R	D	NA
47	R, I	UFU	-
48	N, T	D	2
49	TR, RTO	NA	NA
50	NA	NA	NA
51	NA	NA	NA
52	NA	NA	NA
53	NA	NA	NA
54	R, S, T	UFU	-
55	N, TR, C, R	TGO	-
56	E, S	D	13
57	C, R	D	11
58	C	Fav	-
59	P	D	NA
60	C, R	D	4
61	N	NA	NA
62	S	NA	NA
63	S	D	17
64	P, I	D	11
65	NA	NA	NA
66	N, S	Fav	-

BT: blood transfusion, C: chemotherapy, D: death, Fav: favorable, I: immunotherapy, N: nephrectomy, NA: not available, PR: palliative radiotherapy, R: radiotherapy, RTO: referred to oncologist, S: surgery, T: targetoid therapy, TGO: treatment going on, TR: tumor resection, UFU: under follow-up, VPD: vasopressive drugs

of abundant red marrow in the mandible, whereas the maxilla contains mostly fatty marrow.[7] Abundant receival of blood and release of angiogenic factors and dysfunction of the von Hippel-Lindau gene result in the hypervascularity of these tumors creating a pre-angiogenic environment.[6] Angiogenesis plays a crucial role in the development of tumor metastasis.

The temporomandibular joint (TMJ) is a rare location of metastasis that usually arises in the late stages of cancer that is connected with skeletal metastases. It is thought to be owing to weak red marrow and deficit blood flow from the maxillary and temporal arteries. Furthermore, the presence of a bone plate in the condylar region may limit tumor cell proliferation, resulting in decreased tumor cell entrapment.

JBM is more difficult to diagnose than soft tissue lesions because of their resemblance to SCC, their central location, asymptomatic nature, and nonspecific radiographic features. Furthermore, because the jaws are not frequently inspected at autopsy, some abnormalities may be missed. As a result, the true incidence of metastatic tumors in the jaws may be higher.

JBM is of high clinical importance because it may be the only symptom of an undiagnosed underlying malignancy or the first sign of metastasis. In our study, JB was the initial site of metastasis in 31.8% of cases, whereas, in 16.6% of cases, metastasis was detected after the nephrectomy was performed for RCC, with an average mean time of 35 months.

Clinically, metastatic RCC to JB is characterized by rapidly growing painful or asymptomatic highly vascular palpable

Table 4: Summary of results documented from literature research describing the characteristics of jaw bone metastasis from renal cancer (1939–2022)

Feature	Number
Total number of papers published	56 • Case reports—48 • Case series—2 • Retrospective analysis—6
Total number of patients	66
Worldwide distribution of cases	• USA—18 (27.3%) • Japan—10 (15.1%) • UK—6 (9%) • India—5 (7.6%) • Germany=Iran–4 (6%) • Greece=China—3 (4.5%0 • Spain—2 (3%) • Austria=Brazil=Finland=France=Korea=Maxico=Malaysia=Morocco=Nigeria=Sweden=Turkey—1 (1.5%)
Gender	• M—36 (54.5%0 • F—17 (25.8%) • NA—13 (19.7%) • M: F=2.1:1
Average age of patients (mean, range)	• Total—54.1 Yr. (1–89 Yr.) • M—53.5 Yr. (1–89 Yr.) • F—52.3 Yr. (2.75–81 Yr.)
Previous history of RCC	• Y—10 • N—21 • NA—35
Associated risk factors	• Y—10 (15.2%) • N—9 (13.6%) • NA—47 (71.2%) • HT—4, RD—3, S—2, T—1, A—1
Jaw involved in metastasis	• Mand—49 (74.2%) • (R—8, L—9. NA—32) • (A—5, P—7, NA—37) • Max—14 (21.2%) • (R—1, L—4, NA—8, BL—1) • (A—2, P—3, NA—90 • TMJ condyle—2 (3%) • (R=L—1) • Both jaws—1 (1.5%)
Jaw bone as the initial site of metastasis	• Y—21 (31.8%) • N—11 (16.6%) • NA—34 (51.6%)
Any other site of metastasis	• Y—30 (45.4%0 • N—8 (12.1%) • NA—28 (42.4%)
Average mean time JBM metastasis after nephrectomy	• 35 months (2 Yrs. 11 Mon)
Radiographic appearance	• NA—42 (63.6%0 • OL—17 (25.7%) • Bone resorption—4 (6.1%)
Final diagnosis of metastatic RCC	• CCC–62 (94%) • CCS—2 (3%) • CCP—1 (1.5%) • SCC—1 (1.5%)
Treatment aids	• Combined therapy—15 (27.7%) • Surgery—4 (6.1%) • Chemotherapy—2 (3.3%) • Palliative=nephrectomy=embolization=palliative radiotherapy=1 (1.6%) • NA—41 (62.1%)

Contd...

Table 4: Contd...

Feature	Number
Prognosis	• Deaths—13 (19.7%) • Favorable—2 • UFU—2 (3.3%) • TGO—1 (1.6%) • NA—48 (72.7%)
Average mean time of death from diagnosis of JBM (range)	8.5 Mon (2–17 Mon)

A: anterior, BL: bilateral, CCC: clear cell carcinoma, CCS: clear cell sarcoma, CCP: clear cell papilloma, DM: diabetic mellitus, F: female, HT: hypertension, JBM: jaw bone metastasis, L: left, LFU: lost to follow-up, M: male, Mon: months, N: no, NA: not available, OL: osteolytic, P: posterior, R: right, RCC: renal cell carcinoma, RD: renal diseases, S: smoking, SCC: small cell carcinoma, TGO: treatment going on, Tt: treatment, UFU: under follow-up, UK: United Kingdom, USA: United States of America, Y: Yes, Yr.: years

mass accompanied by difficulty in chewing, dysphagia, paraesthesia, and pathological fractures.[31,32] In the present research, rapidly increasing vascular swelling was the most predominant clinical feature observed. Other features included masses, erythema, dysphagia etc. These metastatic lesions often become difficult to diagnose because their variable appearance bears close resemblance to various inflammatory disorders of the jaw, periapical and odontogenic lesions, and JB tumors. TMJ metastasis can be misinterpreted as TMJ problems. To exclude the primary malignancies of JB, a history of primary metastatic RCC in the patient could be a guiding tool for detecting the secondary deposits. In the current research, 15.2% of patients had a previous history of primary RCC with nephrectomy, while 31.8% of patients did not reveal such history.

The radiographic characteristics of JBM are not pathognomonic. Most malignancies are characterized by osteolysis. Certain tumors can cause reactive new bone development, resulting in a mixed radiopaque and radiolucent lesion. To identify the amount of soft tissue involvement and other sites of distant metastasis in the body, computerized tomography scans and magnetic resonance imaging are required. 25.7% of lesions in the current study manifested as osteolytic, with ill-defined radiolucency. In the majority of cases, radiographic interpretation was missing.

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, RCC has been divided into various subgroups. World Health Organization's classification of urogenital tumors in 2022 has introduced many new entities in the RCC.[40] CCC is the most predominant type and has been discovered to be the most prevalent metastasizing to the JB. Other tools, such as special staining, immunohistochemistry, and electron microscopy, may be necessary for some circumstances to determine the initial tumor's nature. Imaging techniques, such as computerized tomography scans, magnetic resonance imaging, and positron emission tomography, can help in the assessment of possible extension and distant organ metastasis.

Although RCC entails multiorgan distant metastases, JB might occasionally be the only site of metastasis many times. 12.1% of instances in this study had JB as the only location of RCC metastasis, whereas 45.4% had metastasis to other regions as well, such as lungs, brain, adrenals, liver, vertebrae, spine, pelvis, skin, and skeletal muscles (4).

The treatment of choice for primary RCC ranges from partial to radical nephrectomy or cytoreductive therapy. However, options for metastatic RCC to JB include biopsy, surgery, chemotherapy, radiotherapy, brachytherapy, and/or combination therapy. RCC is often resistant to chemotherapy and radiotherapy. The most commonly used therapeutic aids in this study were combination therapy and surgical aid. Unfortunately, metastatic RCC has a bad prognosis with a maximum survival rate of appx 5 yr. In some cases, a patient's terminal stage of disease results in a loss of follow-up or death. However, according to the current study, only 19.7% of individuals died with an average survival time of 8.5 months. 3.3% of patients had a good prognosis with no signs of recurrence. In one patient, treatment is going on. Two cases are under follow-up. These results may be because of the lack of information available in many of the papers included in this review.

LIMITATIONS OF CURRENT RESEARCH

One of the major limitations of our research was the lack of information provided for many parameters included for data extraction.

CONCLUSIONS

During the last 83 years (1939–2022), we found only 66 cases of RCC metastasis to JB. This signifies a rare occurrence of JBM from RCCC. 10.7% of patients died with a mean survival rate of 8.5 years. The mandible was the most affected gland followed

by the maxilla. Because of their resemblance to primary neoplastic and nonneoplastic JB 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 to identify the primary site of metastasis and choose the best course of treatment.

Ethical approval

Not required.

Abbreviations

CCC: clear cell carcinoma, CoCoPop: context, condition, population, tomography, JBs: jaw bones, JBM: jaw bone metastasis, NA: not available, OST: oral soft tissues, PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCC: renal cell carcinoma.

Author's contributions:

SG: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Validation, Writing-original draft, Writing-review & editing. AV, SG, HVP, RS : Investigation, Methodology, Project administration, Validation. MD, MP, AR,FM: Formal analysis, Final review, Supervision

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Abraham G, Cherian T, Mahadevan P, Avinash T, George D, Manuel E. Detailed study of survival of patients with renal cell carcinoma in India. Indian J Cancer 2016;53:572.
3. Padala SA, Barsouk A, Thandra KC, Saginala K, Mohammed A, Vakiti A, *et al*. Epidemiology of Renal Cell Carcinoma. World J Oncol 2020;11:79-87.
4. Brufau BP, Cerqueda CS, Villalba LB, Izquierdo RS, González BM, Molina CN. Metastatic renal cell carcinoma: Radiologic findings and assessment of response to targeted antiangiogenic therapy by using multidetector CT. Radiographics 2013;33:1691-716.
5. Gong J, Maia MC, Dizman N, Govindarajan A, Pal SK. Metastasis in renal cell carcinoma: Biology and implications for therapy. Asian J Urol 2016;3:286-92.
6. Irani S. Metastasis to the Jawbones: A review of 453 cases. J Int Soc Prev Community Dent 2017;7:71-81.
7. Kirschnick LB, Schuch LF, Cademartori MG, Vasconcelos ACU. Metastasis to the oral and maxillofacial region: A systematic review. Oral Dis 2022;28:23-32.
8. Hirshberg A, Berger R, Allon I, Kaplan I. Metastatic tumors to the jaws and mouth. Head Neck Pathol 2014;8:463-74.
9. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, *et al*. CARE guidelines for case reports: Explanation and elaboration document. J Clin Epidemiol 2017;89:218-35.
10. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al*. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344-9.
11. Vogt LG. Hypernephrommetastase unter dem bilde wurzel- zyste im unterkiefer. Roentgenpraxis 1939;11:99-101.
12. Guyot L, Sauvant J, Menasse F. Hemorrhagic mandibular metastasis of renal origin: Usefulness of therapeutic embolization. Presse Med 1999;28:1066-9.
13. Pruckmayer M, Glaser C, Marosi C, Leitha T. Mandibular pain as the leading clinical symptom for metastatic disease: Nine cases and review of the literature. Ann Oncol 1999;9:559-64.
14. Honig JF. Inheritance of Hippel-Lindau disease: A rare case of maxillary bone metastasis. J Craniofac Surg 2000;11:71-3.
15. Zakaria M, Lim Lye Hock K. Renal cell carcinoma metastatic to the mandible. Asian J Oral Maxillofac Surg 2004;16:189-94.
16. Sastre J, Naval L, Muñoz M, Gamallo C, Diaz FJ. Metastatic renal cell carcinoma to the mandible. Otolaryngol Head Neck Surg 2005;132:663-4.
17. Heinroth S, Bilkenroth U, Eckert AW. Bone metastases in the maxilla as first manifestation of renal cell cancer. A case report. Mund Kiefer Gesichtschir 2006;10:42.
18. Jia J, Chen XM, Sun ZJ, Zhang WF. Mandibular metastasis of nephroblastoma: A rare case. Int J Oral Maxillofac Surg 2006;35:1160-1.
19. Muttagi SS, Chaturvedi P, D'Cruz A, Kane S, Chaukar D, Pai P, *et al*. Metastatic tumors to the jaw bones: Retrospective analysis from an Indian tertiary referral center. Indian J Cancer 2011;48:234-9.
20. Kelles M, Akarcay M, Kizilay A, Samdanci E. Metastatic renal cell carcinoma to the condyle of the mandible. J Craniofac Surg 2012;23:e302-3.
21. Murakami K, Yamamoto K, Aoki K, Fukumoto I, Sugiura T, Kirita T. Metastatic sarcomatoid renal cell carcinoma to the mandible treated with Sorafenib. Open J Stomatol 2012;2:222-7.
22. Ahmadnia H, Amirmajdi NM, Mansourian E. Renal cell carcinoma presenting as mandibular metastasis. Saudi J Kidney Dis Transpl 2013;24:789-92.
23. Jallu A, Latoo M, Pampori R. Rare case of renal cell carcinoma with mandibular swelling as primary presentation. Case Rep Urol 2013;2013:806192.
24. Zhang L, Yang H, Zhang X. Metastatic renal cell carcinoma to the jaws: Report of cases. World J Surg Oncol 2014;12:204.
25. Liuzzi J, Dacunha M, Siso S, Garriga E. A Rare case of a renal cell carcinoma metastasizing to the mandible as primary presentation. Arch Surg Oncol 2015;1:1
26. Shah A, Jahan S, Najar L, Hassan S, Mohammad M. Metastatic clear cell variant of renal cell carcinoma of the mandible: Review and case report. Ann Maxillofac Surg 2016;6:144-7.
27. Gooran S, Fakhr Yasseri A, Behtash N, Karimi A, Khalili M, Asadi M. Mandibular mass as an only presentation of metatatic renal cell carcinoma for four years: A case report. Urol J. 2017;14:2979-81.
28. Lieder A, Guenzel T, Lebentrau S, Schneider C, Franzen A. Diagnostic relevance of metastatic renal cell carcinoma in the head and neck: An evaluation of 22 cases in 671 patients. Int Braz J Urol 2017;43:202-8.
29. Derakhshan S, Rahrotaban S, Mahdavi N, Mirjalili F. Metastatic renal cell carcinoma presenting as maxillary lesion: Report of two rarecases. J Oral Maxillofac Pathol 2018;22:S39-43.
30. Ardhaoui H, Halily S, Abada R, Rouadi S, Roubal M, Mahtar M.

Mandibular metastasis revealing a clear cell renal cell carcinoma. Glob J Oto 2019;19:556006.
31. Netto R, de Freitas Filho SAJ, Cortezzi W, Merly F, de Andrade VM, Pires FR. Metastasis of renal cell carcinoma causing significant facial asymmetry. Case Rep Surg 2019;2019:6840873.
32. E Bassey IA, Isiwele E, Ugbem T, Anyaechi C, Okonkwo SN, Essiet SA. Renal cell carcinoma metastasizing to the head and neck: A case report and literature review. East African Scholars J Med Sci 2020;3:351-4.
33. Ludwig DC, Garcia J, Chang OH, Closmann JJ. Metastatic renal cell carcinoma to the mandible: A case report with clinical and histologic findings. Gen Dent 2020;68:41-4.
34. Nishii N, Shimamoto H, Ohsako T, Yokokawa M, Sato Y, Ohata Y, *et al*. Renal cell carcinoma metastasis to the maxillary bone successfully treated with surgery after vascular embolization: A case report. J Med Case Rep 2020;14:193.
35. Zhang R, Lee CW, Basyuni S, Santhanam V. Mandibular swelling as the initial presentation for renal cell carcinoma: A case report. Int J Surg Case Rep 2020;70:96-100.
36. Paraskevopoulos K, Vahtsevanos K, Ntomouchtsis A, Kalaitsidou I, Patrikidou A, Andreadis C, *et al*. Metastatic tumors to the oral cavity-A retrospective analysis. Int Res J Otolaryngol 2021;4:10.
37. Jung SY, Maeng JY, Lee H, Han JJ, Kim SM, Myoung H. Metastasis of renal cell carcinoma to the mandible. J Craniofac Surg 2023;34:e334-6.
38. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, *et al*. SEER Cancer Statistics Review 1975-2016. Bethesda: National Cancer Institute; 2019. Available from: https://seer.cancer.gov/csr/1975_2016/. [Last accessed 2020 Apr 09].
39. Tsivian M, Moreira DM, Caso JR, Mouraviev V, Polascik TJ. Cigarette smoking is associated with advanced renal cell carcinoma. J Clin Oncol 2011;29:2027-31.
40. Moch H, Amin MB, Berney DM, Compérat EM, Gill AJ, Hartmann A, *et al*. The 2022 World Health Organization classification of tumours of the urinary system and male genital organs—Part A: Renal, penile, and testicular tumours. Europ Urol 2022;82:458–68.