



Original Research Article

The Role of Oral and Maxillofacial Surgeons in the Early Detection of Multiple Myeloma: A Systematic Review

Article History:

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Abstract: **Background:** Multiple myeloma (MM) is a malignant plasma cell neoplasm with both systemic and oral manifestations. Oral lesions may precede systemic symptoms, providing an opportunity for early detection. **Objective** To systematically summarize the role of OMFS in the early recognition of MM through clinical and radiographic oral findings. **Methods** A systematic literature search of PubMed (2005–2025) was conducted using the keywords “multiple myeloma” AND “oral manifestation.” Inclusion criteria were case reports, cohort studies, and cross-sectional studies reporting oral and radiographic manifestations of MM. Reviews, narrative articles, non-English publications, and studies lacking validated clinical or radiographic descriptions were excluded. Data on oral features, radiographic findings, systemic CRAB criteria, and OMFS interventions were extracted. Methodological quality was assessed using a standardized risk of bias tool, following PRISMA 2020 guidelines. **Results** Twenty studies were included. Oral manifestations were diverse, with swelling (55%), jaw pain (30%), soft tissue masses (25%), gingival enlargement (25%), dental mobility (20%), and paresthesia (15%) most frequently reported. Radiographically, punched-out osteolytic lesions were observed in 12 studies, predominantly affecting the posterior mandible. Systemic features frequently aligned with CRAB criteria, including bone pain, anemia, fatigue, and recurrent infections. OMFS interventions facilitated timely hematology referral, imaging, biopsy, and prevention of bisphosphonate-related osteonecrosis. **Conclusions** Early recognition of oral and radiographic manifestations by OMFS enables prompt referral and multidisciplinary management, improving patient outcomes. Incorporating vigilant oral assessments into routine practice enhances early diagnosis and prognosis in MM patients.

Keywords: Bone Pain, Jaw Lesions, Multiple Myeloma, Punched-Out Lesions, Gingival Enlargement, Soft Tissue Masses.

INTRODUCTION

The term "multiple myeloma" (MM) originated by J. Von Rustizky in 1873 after he identified eight distinct bone marrow malignancies, while Samuel Solley documented the earliest well-characterized case in 1844 (1). Multiple myeloma is a malignant B-cell neoplasm characterized by clonal proliferation of plasma cells within the bone marrow, leading to abnormal immunoglobulin production and secretion (2). This disorder is associated with diverse

complications, including immunodeficiency, renal failure, anemia, and bone destruction (3). The disease predominantly affects individuals over the age of 40, with a higher incidence in males (4,5).

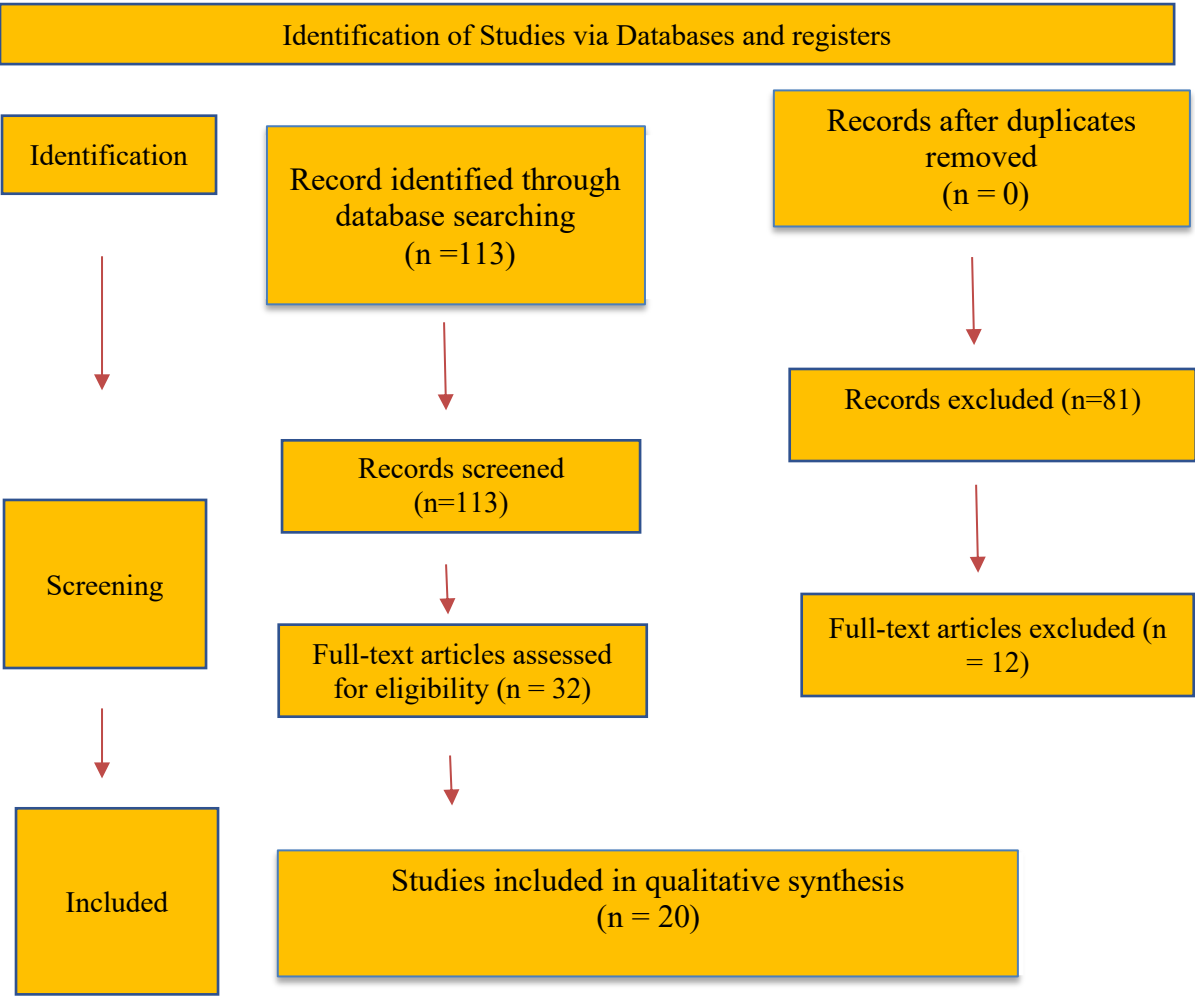
Multiple myeloma is defined by multifocal proliferation of atypical plasma cells and the presence of monoclonal immunoglobulins, commonly referred to as M-proteins or myeloma proteins (6). These M-proteins consist of heavy and light chains, with IgG being the most frequent (52%), followed by IgA (21%), IgD (2%), IgM (0.5%), and light chains alone (16%) (7). Osteolytic lesions occur in over 30% of patients, and oral manifestations may serve as the initial presentation in approximately 14% of cases (8). The prevalence of primary jaw involvement ranges from 8% to 15%, predominantly affecting the mandibular molar region, ramus, and angle due to their high hematopoietic activity, while maxillary lesions are more commonly observed in the posterior regions (9,10).

Clinically, patients with MM frequently present with persistent bone pain, recurrent infections, fatigue, and multisystem involvement (11). The disease is further characterized by end-organ damage, summarized by the CRAB criteria, which includes hypercalcemia, renal insufficiency, anemia, and bone lesions (12). Despite being the second most frequent bone marrow malignancy, MM constitutes only 2% of all cancers and 10% to 15% of hematologic malignancies (5). The disease may present as a solitary plasmacytoma or as multiple lesions affecting various skeletal sites, including the spine, skull, pelvis, sternum, vertebrae, and ribs (13). Unlike other metastatic bone tumors, osteolytic lesions in MM do not trigger reactive bone formation (14). Common clinical manifestations include bone pain, pathologic fractures, fatigue, recurrent infections, and secondary amyloidosis, with radiographs often revealing diffuse or localized osteolytic lesions or ‘punched out’ lesions (15). Early diagnosis facilitates timely initiation of therapy, improving patient prognosis. Current treatment strategies include corticosteroids, bisphosphonates, chemotherapy, and hematopoietic stem-cell transplantation, with disease staging and prognosis guided by the International Staging System. Oral health is a critical yet often overlooked aspect of MM management, as systemic symptoms may adversely impact the oral cavity, particularly the gingival tissues. Dentists should be vigilant for oral manifestations, as it will help to identify early indication of disease and its progression.

METHODOLOGY

This systematic review followed the PRISMA 2020 guidelines (16). A comprehensive literature search was conducted in PubMed. Hence, studies published between 2005 and 2025 were included to ensure contemporary diagnostic, radiographic, and therapeutic relevance, using the keywords “multiple myeloma” AND “oral manifestation.” Boolean operators and MeSH terms were applied to enhance sensitivity. After retrieval, duplicates were removed, and titles and abstracts were screened. Exclusion criteria included reviews, systematic reviews, narrative articles, non-English language publications, and studies lacking validated clinical or radiographic descriptions. Full texts of potentially eligible studies were assessed for inclusion. Data extraction included author, year, country, study type, oral manifestations, radiographic findings, systemic symptoms, and diagnostic outcomes. Methodological quality was assessed using a standardized risk of bias tool, with studies categorized as high, moderate, or low quality as shown in figure 1.

FIGURE 1: PRISMA FLOW DIAGRAM FOR SYSTEMATIC REVIEW



RESULTS

Following screening and eligibility assessment, 20 studies (2005–2025) met the inclusion criteria and were included in the qualitative synthesis. Most were case reports (70%), followed by cohort and cross-sectional studies (10% each), with one retrospective cohort study and one case series (5% each). No randomized controlled trials were identified, highlighting the rarity of oral-first presentations of Multiple Myeloma. Oral manifestations were diverse and frequently represented the initial sign of systemic disease. The most common presentation was jaw swelling, predominantly in the posterior mandible. Other findings included gingival enlargement, soft tissue masses, paresthesia, dental mobility, ulceration, gingival bleeding, and epistaxis often mimicking common odontogenic conditions. Radiographically, multiple osteolytic “punched out” lesions were the characteristic feature, mainly affecting the mandible. Additional findings included localized radiolucency’s, diffuse bone destruction, and occasional temporomandibular joint involvement as shown in table 1.

Table 1. Characteristics of Included Studies Reporting Oral Manifestations of Multiple Myeloma (n = 20)

S. No	First Author (Year)	Study Design	Key Oral Manifestations
1	Feitosa et al., (2020) (17)	Cross-sectional	• Pale mucosa • Swelling • Facial palsy • Osteonecrosis • Petechiae
2	Almeida et al., (2018) (18)	Case report/series	• Pain • Bleeding • Dysphagia • Paresthesia • Osteolytic lesions
3	Pereira Hansen et al., (2018) (19)	Case report	• Gingival mass
4	Thomas et al., (2015) (20)	Case report	• Facial swelling • Limited mouth opening
5	Bezerra et al., (2021) (21)	Cross-sectional	• Oral health alterations in MM patients
6	Romano et al., (2014) (22)	Case report	• Oral lesion as first manifestation
7	Ali et al., (2018) (23)	Case report	• Swelling • Odontalgia • Paresthesia • Dental mobility • Gingival hemorrhage • Ulceration • Punched-out lesions
8	Vieira-Leite et al., (2008) (24)	Case report	• Mandibular lesion as initial presentation
9	Goetze et al., (2015) (25)	Case report	• Osseous mandibular plasmacytoma
10	Beaumont et al., (2021) (26)	Case series	• Oral masses mimicking benign lesions
11	Vinayachandran et al., (2013) (27)	Case report	• Multiple osteolytic lesions
12	Pushpanshu et al., (2014) (28)	Case report	• Mandibular mass
13	Souza et al., (2021) (29)	Cohort study	• Pain • Paresthesia • Jawbone involvement
14	Kasamatsu et al., (2015) (30)	Case report	• Diffuse swelling • Multiple punched-out radiolucency
15	Owotade et al., (2005) (31)	Cohort study	• Swelling • Epistaxis • Gingival bleeding
16	Abboud et al., (2016) (32)	Retrospective cohort	• TMJ lesions • TMJ dysfunction
17	Zhao et al., (2014) (33)	Case report	• Painful ulcer-like maxillary mass • Bone pain
18	Crowley et al., (2016) (34)	Case report	• Mandibular pain • 2 cm lytic lesion
19	Jain et al., (2013) (35)	Case report	• Generalized gingival enlargement
20	Ramaiah et al., (2015) (36)	Case report	• Maxillary alveolar mass • Tooth mobility

Swelling was the most reported oral feature, observed in over half of studies. Other frequent findings included jaw pain, soft tissue masses, gingival enlargement, dental mobility, and paresthesia. Rare manifestations, such as osteonecrosis, TMJ involvement, and severe intraoral hemorrhage, were reported in only one study each, highlighting the spectrum of oral presentations as shown in table 2.

Table 2. Frequency Distribution of Reported Oral Manifestations (n = 20 studies)

Oral Manifestation	Number of Studies Reporting	Percentage (%)
Swelling (mandible/maxilla)	11	55
Gingival enlargement / hyperplasia	5	25
Gingival bleeding	4	20
Soft tissue mass	5	25
Dental mobility	4	20
Paresthesia	3	15
Jaw pain	6	30
Ulceration	2	10
Osteonecrosis of jaw	1	5
TMJ involvement	1	5
Intraoral hemorrhage	1	5

Punched-out osteolytic lesions were the main radiographic finding, mainly in the posterior mandible. Other features, including cortical bone destruction, localized radiolucency, diffuse radiolucent lesions, TMJ involvement, and larger lytic lesions, were less frequent. Panoramic radiographs and CBCT were the primary imaging modalities as shown in table 3.

Revised Table 3: Radiographic Findings in Multiple Myeloma Affecting the Jaw (n = 20 studies)

Radiographic Feature	Number of Studies	Common Location	Frequency
Punched-out osteolytic lesions	12	Posterior mandible	High
Localized radiolucency	5	Mandible	Moderate
Cortical bone destruction	4	Mandibular angle/ramus	Moderate
TMJ lesions	1	TMJ	Rare
Diffuse radiolucent lesion	2	Maxilla	Rare
Lytic Lesion (≥ 2 cm)	3	Mandible	Low

Systemic manifestations accompanying oral lesions frequently aligned with CRAB criteria. Bone pain and anemia were the most reported, followed by fatigue, recurrent infections, hypercalcemia, renal insufficiency, and weight loss, underscoring the systemic impact of MM as shown in table 4.

Table 4. Systemic Manifestations Associated with Oral Presentation (CRAB Criteria, n = 20 studies)

Systemic Feature	Frequency (Studies)
Bone pain	7
Anemia	5
Fatigue	4
Hypercalcemia	2
Recurrent infections	3
Renal insufficiency	2
Weight loss	1

The posterior mandible was the most frequently affected site, reflecting high hematopoietic marrow activity. Other less frequent sites included the mandibular angle/ramus, posterior maxilla, gingiva, TMJ, and diffuse jaw involvement, demonstrating variable lesion distribution as shown in table 5.

Table 5. Anatomical Distribution of Oral Lesions (n = 20 studies)

Site of Involvement	Number of Studies	Percentage (%)
Posterior mandible	11	55
Mandibular angle/ramus	5	25
Maxilla (posterior)	6	30

Site of Involvement	Number of Studies	Percentage (%)
Gingiva	5	25
TMJ	1	5
Diffuse jaw involvement	3	15

Most studies were case reports, reflecting the limited high-level evidence available on oral-first presentations of MM as shown in table 6.

Table 6. Distribution of Study Designs (n = 20)

Study Type	Number of Studies	Percentage (%)
Case reports	14	70
Case series	1	5
Cohort studies	2	10
Cross-sectional studies	2	10
Retrospective cohort	1	5

Overall, the included studies demonstrated moderate risk of bias due to small sample size, lack of controls, retrospective designs, and limited follow-up, which may affect generalizability as shown in table 7.

Table 7. Risk of Bias Assessment

Study Type	Risk of Bias Level	Common Limitation
Case reports	Moderate–High	Small sample size
Case series	Moderate	Lack of control group
Cohort studies	Moderate	Retrospective design
Cross-sectional studies	Moderate	Limited longitudinal data
Retrospective cohort	Moderate	Limited sample size, retrospective

Early recognition of unexplained swelling, punched-out lesions, gingival bleeding, and paresthesia by OMFS facilitated timely referral, imaging, biopsy, and lab evaluation. Pre-bisphosphonate dental assessments helped prevent osteonecrosis, highlighting the critical contribution of dental specialists in MM diagnosis and management as shown in table 8.

Table 8. Role of Oral & Maxillofacial Surgeons (OMFS) in Diagnostic Pathway

OMFS Intervention	Clinical Impact
Recognition of unexplained swelling	Triggered hematology referral
Identification of punched-out lesions	Prompted imaging & biopsy
Detection of gingival bleeding	Laboratory evaluation
Recognition of paresthesia	Consideration of MM in differential
Pre-bisphosphonate dental assessment	Prevention of osteonecrosis

DISCUSSION

Multiple myeloma (MM) often presents with oral and maxillofacial manifestations that may precede systemic diagnosis (37). In this review of 20 studies, jaw swelling was the most frequently reported feature (55%), followed by jaw pain (30%), soft tissue masses (25%), and gingival enlargement (25%) (38, 39). Dental mobility (20%) and paresthesia (15%) were also observed, highlighting the diverse oral presentations of MM. Rare manifestations, including osteonecrosis, TMJ involvement, and severe intraoral hemorrhage, were reported in individual studies, reflecting the spectrum of clinical findings.

Radiographically, punched out osteolytic lesions were the main finding, identified in 12 studies, primarily affecting the posterior mandible (39, 40). Additional imaging findings included localized radiolucency's, diffuse bone destruction, TMJ lesions, and larger lytic lesions, demonstrating the importance of panoramic radiography and CBCT for early detection. Anatomically, the posterior mandible was the most frequently affected site (55%), followed by posterior maxilla (30%) and mandibular angle/ramus (25%) (41).

Systemic features accompanying oral manifestations were consistent with CRAB criteria. Bone pain (7 studies), anemia (5), fatigue (4), and recurrent

infections (3) were the most frequently reported systemic signs (38, 40). These findings emphasize the need for oral health professionals to consider MM in the differential diagnosis when patients present with unexplained oral lesions, particularly in the posterior jaw.

This systematic review provides a comprehensive synthesis of oral and radiographic manifestations of multiple myeloma, emphasizing the critical role of OMFS in early detection. Strengths of this review include the inclusion of contemporary studies spanning 2005–2025, strict adherence to PRISMA 2020 guidelines, detailed extraction of clinical, radiographic, and systemic features, and structured presentation of data through tables summarizing prevalence, anatomical distribution, and OMFS interventions. The review also highlights practical implications for timely diagnosis, referral, and prevention of complications such as bisphosphonate-related osteonecrosis. However, several limitations must be acknowledged. Most included studies were case reports or cohorts, limiting generalizability and introducing potential publication bias. Heterogeneity in study designs, reporting standards, and diagnostic criteria restricted the ability to perform quantitative synthesis. Moreover, the absence of randomized controlled trials and longitudinal studies limits conclusions regarding the predictive value of oral manifestations for systemic disease progression. Despite these limitations, this review provides valuable insights into early oral presentations of MM and underscores the importance of vigilant oral assessments in clinical practice.

Conclusion

Oral manifestations often precede systemic signs of multiple myeloma. Early recognition by oral and maxillofacial surgeons facilitates timely diagnosis, referral, and prevention of treatment complications, underscoring the critical role of dental professionals in multidisciplinary management.

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