*Yuhong Lin, DDS,[*] Vivek Thumbigere-Math, BDS, PhD,[†] Anil Kishen, BDS, MDS, PhD,[‡] and Jianing He, DMD, PhD[*]*

REVIEW ARTICLE

# Unraveling the Etiology and Pathogenesis of Multiple Cervical Root Resorption – A Scoping Review

## SIGNIFICANCE

Systemic diseases and medications play a significant role in the development of MCRR. An interdisciplinary approach is essential for the prevention, early detection, and personalized management of MCRR to minimize the risk of extensive tooth loss and improve patient outcomes.

## ABSTRACT

**Introduction:** Multiple Cervical Root Resorption (MCRR) is a rare condition characterized by the progressive destruction of the cervical region of multiple tooth roots, leading to significant tooth loss. The etiology and pathogenesis of MCRR remain poorly understood. Existing knowledge is largely derived from case reports/series. A comprehensive review of literature is crucial to identify potential systemic and dental factors that contribute to the development and progression of MCRR. **Methods:** A scoping review was conducted following PRISMA guidelines. Five major health science databases were systematically searched to capture all reported cases of MCRR published to date. Potential etiologic factors were identified and categorized based on their association with MCRRs. **Results:** A total of 65 reports documenting 101 patients and involving 921 teeth were included in the analysis. The review identified several potential etiologic factors, including skeletal disorders, autoimmune diseases, viral infections, genetic diseases, specific genetic mutations, liver dysfunctions, the use of antiresorptive medications, and endocrine disturbances. Each of these factors may influence osteoclast/odontoclast functioning, implicating them in the pathogenesis of MCRR. **Conclusions:** Systemic diseases and medications that alter bone remodeling process or osteoclast/odontoclast function play a significant role in the development of a large proportion of MCRR cases. Given the complex and multifactorial nature of this condition, an interdisciplinary approach involving general dentists, specialists, and physicians is essential. Early detection, prevention, and personalized management of MCRR are critical in minimizing the risk of extensive tooth loss and improving patient outcomes. *(J Endod 2025;51:674–686.)*

## KEY WORDS

Cervical root resorption; etiology; external root resorption; odontoclast; scoping review; tooth resorption

Root resorption of permanent teeth is a complex pathologic process that leads to the progressive destruction of tooth structure. It is broadly classified into internal and external root resorption. Internal resorption is relatively rare and is typically associated with chronic inflammation of the dental pulp[1]. It occurs when the protective predentin layer is damaged, allowing odontoclasts to initiate resorption from within the root canal space and expand outward. In contrast, external root resorption originates on the outer surface of the tooth progressing inward. When external root resorption occurs at the cervical region, it is termed External Cervical Resorption (ECR). The precise etiology of ECR remains unclear, but local factors such as trauma, orthodontic forces, excessive occlusal forces, periodontal surgery, and extraction of neighboring teeth are believed to play a role in the initiation of the resorptive process[2-4]. These factors are thought to disrupt the protective cementum layer on the cervical root surface, making it vulnerable to resorption by odontoclasts. ECR is relatively rare, with a prevalence ranging from 0.46% to 2.2% among patients seeking endodontic care[5-7]. However, its clinical impact is profound due to its insidious nature, which can lead to substantial loss of tooth structure.

When ECR affects 3 or more teeth in the dentition, it is referred to as Multiple Cervical Root Resorption (MCRR)[8,9]. Compared to local factors, MCRR is more likely associated with systemic conditions and medications that affect the entire dentition. Recent advancements in our understanding of molecular biology of bone and root resorption have shed light on the potential etiology of MCRR[10].

From the *Department of Endodontics, Texas A&M University College of Dentistry, Dallas, Texas; †Division of Periodontology, University of Maryland School of Dentistry, Baltimore, Maryland; and ‡The Kishen Lab, Dental Research Institute, Faculty of Dentistry, University of Toronto, Toronto, Ontario, Canada

Address requests for reprints to Jianing He, Department of Endodontics, Texas A&M University College of Dentistry, 3302 Gaston Ave., Dallas, TX 75246.
E-mail address: hejianing@tamu.edu
0099-2399/$ - see front matter


https://doi.org/10.1016/j.joen.2025.02.012

Several systemic conditions, including autoimmune disorders, endocrine disturbances, and viral infections, have been implicated in the development of MCRR[9,11,12]. Additionally, certain medications that affect bone metabolism, such as bisphosphonates and denosumab, have been linked to the onset and progression of MCRR[13,14]. Genetic predispositions, including mutations in genes that regulate bone remodeling, such as those affecting RANK/RANKL/OPG signaling pathways, are believed to contribute to an imbalance in resorptive activity in both bone and tooth structures[10,15,16].

MCRR lesions are often asymptomatic and diagnosed incidentally during routine dental examinations[5,17]. Radiographic imaging typically reveals significant loss of tooth structure by the time MCRR is diagnosed. As a result, treatment options for advanced MCRR are limited. Restorative treatment may be insufficient, and extraction often becomes the only viable option. MCRR can lead to severe consequences such as loss of multiple teeth, even resulting in edentulism. Therefore, prevention and early intervention remain critical, highlighting the importance of understanding the etiology and pathogenesis of MCRR. In-depth analysis of medical and family histories of affected patients can aid in identifying potential causative factors, enabling a more targeted and personalized approach for patient management. A comprehensive understanding of the underlying molecular mechanisms is essential for advancing both diagnosis and treatment. By identifying the systemic and genetic factors contributing to MCRR, clinicians can refine diagnostic protocols and develop new therapeutic interventions aimed at improving patient outcomes and preserving dental integrity, ultimately enhancing the quality of life of affected individuals.

Due to the rare occurrence of MCRR, there are currently no large-scale prospective or retrospective cohort studies available to inform diagnostic and treatment interventions. The existing body of knowledge is primarily derived from case reports and small case series. Due to these limitations, it is not feasible to conduct a systematic review to address the current knowledge gaps in etiology, pathogenesis, and treatment interventions. Instead, a scoping review is deemed more appropriate to comprehensively examine and outline the available evidence, identify knowledge gaps, and provide a direction for future research[18].

Thus, the objectives of this scoping review are to review all MCRR cases reported to date in the literature to – (1) Identify significant dental, medical, and genetic factors associated with the development and progression of MCRR; (2) categorize reported cases based on their potential etiologies; and (3) discuss the possible pathogenesis mechanisms of MCRR based on emerging evidence. By addressing these objectives, this scoping review aims to enhance the understanding of MCRR and facilitate the development of effective diagnostic and therapeutic strategies.

## MATERIALS AND METHODS

The review protocol was drafted in accordance with PRISMA guidelines for scoping reviews. The search strategy was carefully refined following consultations with an experienced health-science librarian and detailed discussions with the review team. Between June and October 2024, a comprehensive search was performed across 5 major health sciences databases: MEDLINE (Ovid), Embase (Ovid), Dentistry & Oral Sciences Source (Ebsco), CINAHL (Ebsco), and Cochrane CENTRAL to identify all relevant literature. The final search results were imported into Covidence for screening, where duplicate references were automatically removed. Additionally, a manual citation search of relevant reviews and literature supplemented the electronic database search to ensure comprehensive coverage. Calibration meetings among reviewers were held biweekly to ensure adherence to the scoping review's objectives. Two independent reviewers screened the titles, abstracts, and full texts of all identified studies based on predefined inclusion criteria. Clinical pictures and radiographs were reviewed when available, to confirm both the location of the resorption site and the number of teeth involved. The literature search process is illustrated in Figure 1.

Inclusion criteria were as follows: (1). Reports describing/discussing MCRR cases affecting permanent teeth in pediatric or adult populations; (2). Cases in which cervical resorption involving at least 3 teeth could be confirmed; and (3). Publications written in English and published between 1930 and October 2024.

For data extraction, a collaborative approach was employed. Two reviewers jointly developed a customized extraction template to ensure a comprehensive and reliable extraction process. Key data points extracted included: (1). Study details (eg, title, authors, country of origin, and year of publication); (2). Patient characteristics (eg, age, gender, medical history, medication use, blood tests, genetic testing, and dental history); (3). Number of MCRR affected teeth; (4). Clinical, radiographic, and histologic characteristics of MCRR affected teeth; and (5). Treatment and management strategies of MCRR affected teeth. Data from the extraction template were exported to Excel for further analysis. Studies sharing similar etiological factors were grouped for detailed evaluation.

## RESULTS

The initial search across 5 databases yielded 628 publications, with an additional 18 publications identified through manual search of reference lists. After removing 333 duplicate records, the abstracts of the remaining 313 papers were screened. Of these, 204 studies were excluded due to irrelevance. For example, titles or abstracts that did not describe a case report or case series were excluded. Titles or abstracts that did not mention "resorption" or distinctly indicated apical resorption or internal resorption instead of cervical resorption were excluded. The full texts of the remaining 109 publications were carefully examined, and 65 met the inclusion criteria and were included in this review.

### Publication Characteristics

Among the 65 case reports and case series included in this scoping review, 14 were published before 1994. Since then, there has been a notable increase in publications over the past 3 decades, with 2 publications between 1995 and 2004, 17 between 2005 and 2014, and 32 between 2015 and 2024 (Fig. 2*A*). Geographically, Europe accounted for the largest proportion of reports (34%), followed by Asia (29%), and North America (26%). The remaining cases originated from Australia (5%), South America (3%), and the Middle East (3%) (Fig. 2*B*).

### Patient Characteristics

A total number of 101 cases involving 921 teeth were described across 65 reports. The gender distribution was nearly equal, with 52% involving females and 48% involving males (Fig. 3*A*). Age-wise, 53% of cases were diagnosed in individuals younger than 30 years of age, 22% were between the ages of 30 to 49 years, and 25% were over the age of 50 years (Fig. 3*B*).

### Etiologic Factors

The potential etiologic factors associated with MCRR are grouped and summarized in Table 1 and Figure 4. Systemic diseases affecting the skeletal system were identified in 10 reports involving 37 patients. These conditions included familial expansile osteolysis (FEO)[19-21], Gorham-Stout Syndrome (GSS)[22], Paget's disease[23], osteoporosis[24-26], osteopenia[27], and osteogenesis imperfecta[28]. Autoimmune diseases such as systemic sclerosis

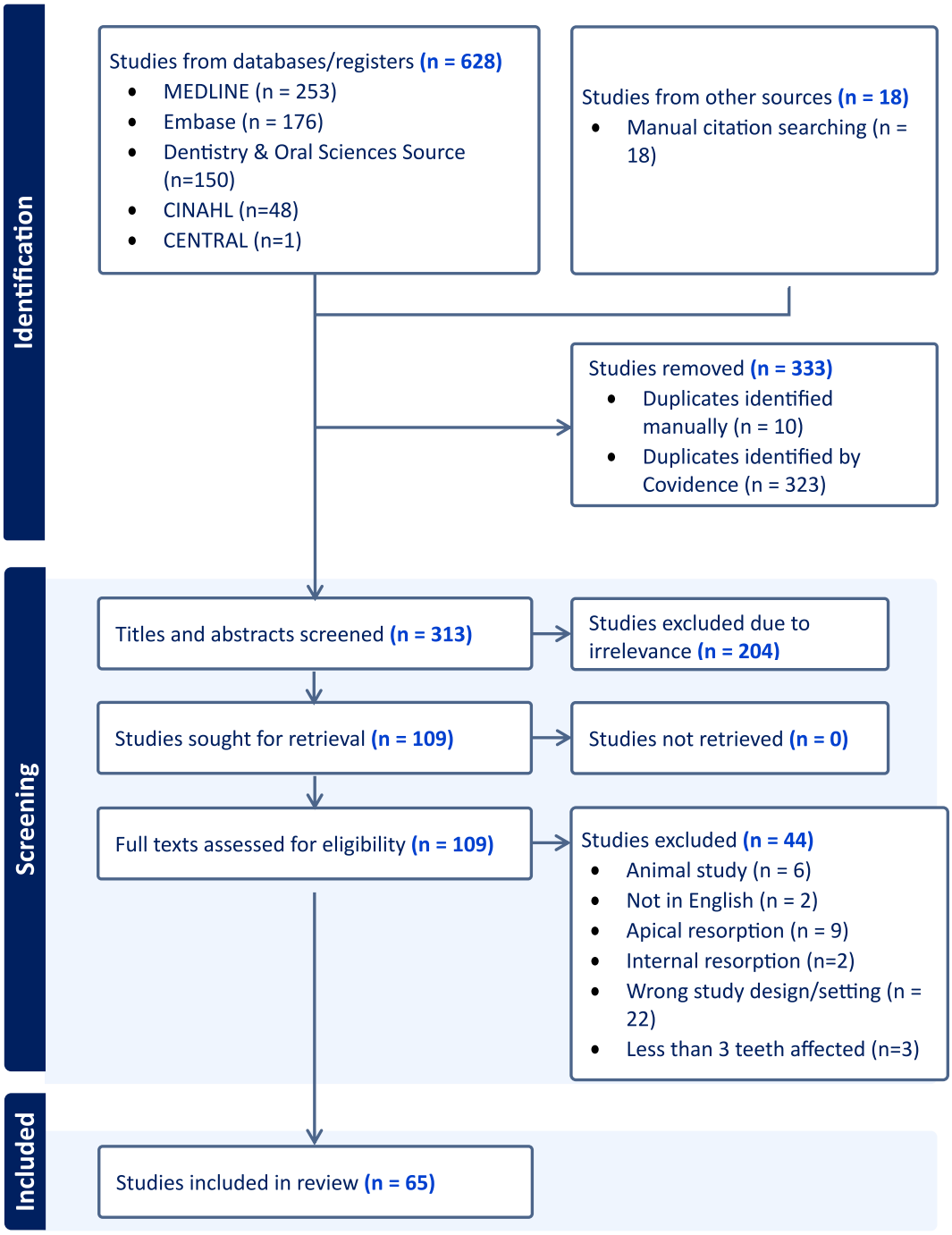


**FIGURE 1 –** Flow diagram of the literature search and included studies.

(SSc)[11,29-31], celiac disease[32], and rheumatoid arthritis[33] were identified in 6 reports. Viral infections, including feline herpes[12] and pertussis,[34] were noted in 2 reports affecting 5 patients. Four cases were linked to the use of antiresorptive drugs including bisphosphonates[35] and denosumab[13,14,36]. Genetic disorders such as Noonan syndrome[37], primary hyperoxaluria[38,39], and hereditary hemorrhagic telangiectasia[40] were reported in 4 cases. Six additional reports identified genetic mutations in affected individuals, who were otherwise healthy[10,15,16,41-43]. Chemotherapy[44], graft vs host disease[45], and benign tumor of the maxilla (inflammatory myofibroblastic tumor)[46] have been suggested to play a role in 3 separate reports. Liver diseases[47,48] and pregnancy[9,49] were the only significant medical history identified in 4 reports. Possible involvement of local factors such as improper at-home bleaching[50], bruxism[27,51,52], malocclusion[53,54], and oral surgery[55] were documented in 6 cases. In the remaining 22 reports, no significant systemic or local contributing factors could be identified, and they were categorized as "idiopathic"[25,27,56-74].

## DISCUSSION

Although MCRR is a relatively rare condition, it can progress rapidly, leading to the loss of multiple teeth and significantly impacting patients' quality of life. Understanding the

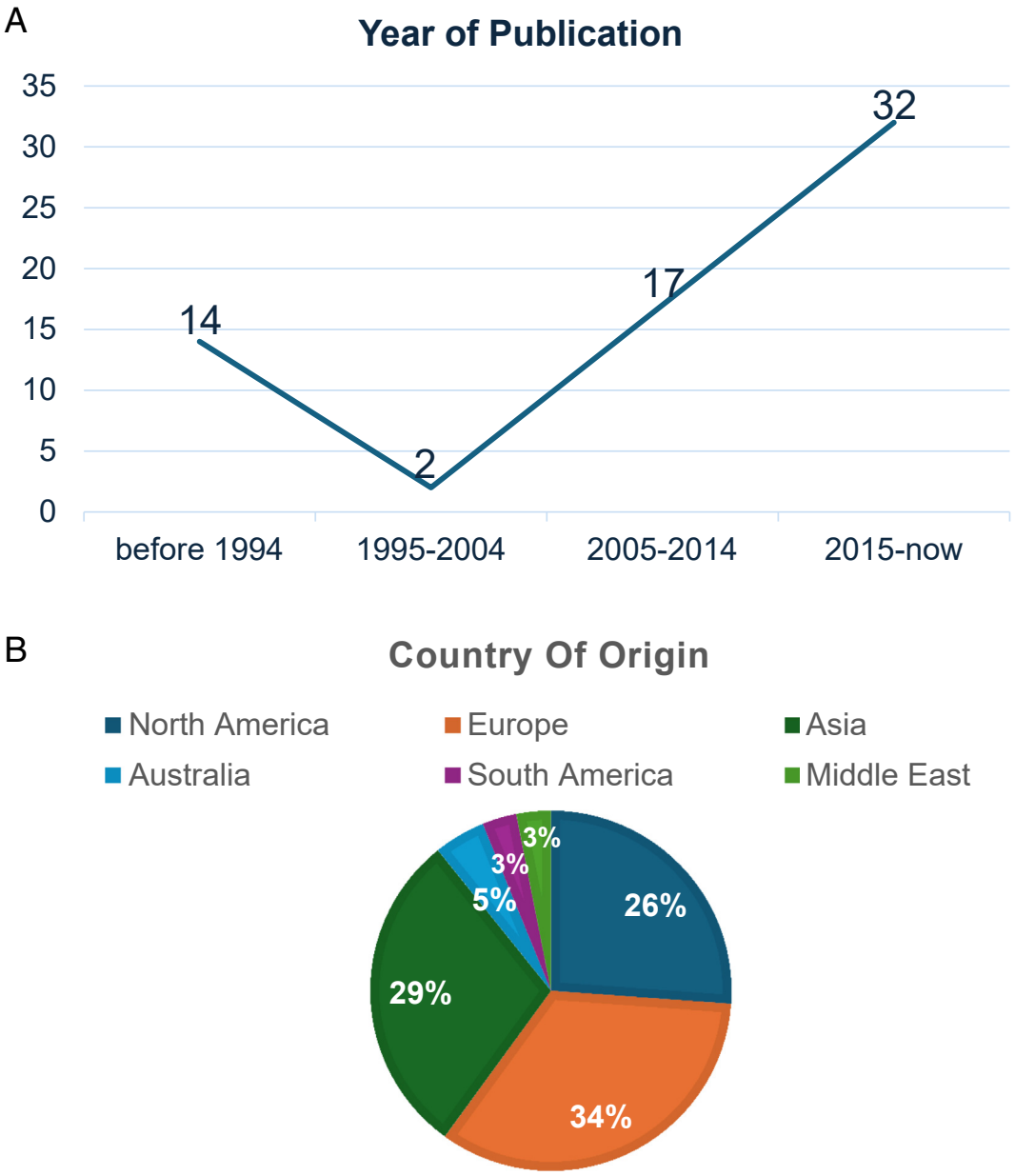


**FIGURE 2 –** Characteristics of publications included. *A*, Year of publication; *B*, Country of origin.

etiology and identifying risk factors is critical for developing effective prevention and treatment strategies for MCRR. However, current knowledge of MCRR is primarily derived from case reports and small case series due to its low prevalence. A comprehensive analysis of these cases is essential to identify systemic and dental etiologic factors contributing to MCRR. This scoping review employed a robust search strategy to capture all qualified cases of MCRR reported in the literature to date. Each full-text article was carefully examined to ensure that the cases met the diagnostic criteria for MCRR. Relevant information from each article, including patient demographics, clinical characteristics, and medical and dental history, was meticulously extracted, compiled, and analyzed.

Overall, 65 publications describing 101 MCRR cases and involving 921 teeth were included. A prior review by Liang et al in 2003 covered 10 studies with 14 affected patients[27], while a 2022 review by Wang et al. reported 36 studies involving 47 cases[8]. However, 4 of these 36 studies could not be retrieved from any health science databases and thus were excluded from the current analysis. Our review identified a substantially higher number of cases compared to the previous reviews. This can be attributed to the increased number of publications in recent years, an enhanced search strategy, and a meticulous examination of the references cited in previous reports. While the 2 previous reviews primarily focused on the clinical and radiographic features and management of MCRR[8,27], with minimal discussion on potential etiologic factors, the current review specifically emphasizes the underlying causes and risk factors of MCRR.

Since all included publications are case reports or case series, no established checklist or criteria can be applied to assess the quality and risk of bias for each report. However, it needs to be noted that while all included reports provided clinical and radiographic documentation to support the diagnosis of MCRR, there are large variations in the amount of details included regarding the medical and

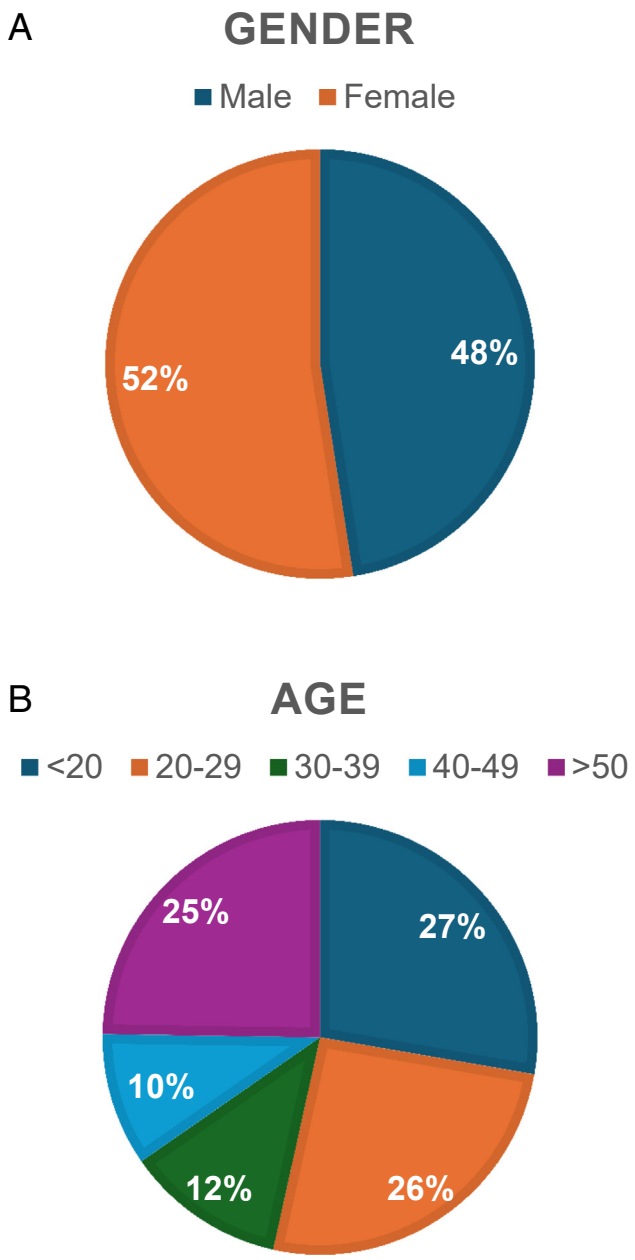


**FIGURE 3 –** Characteristics of patients included. *A*, Gender distribution; *B*, Age distribution.

dental history, blood test, and genetic testing results among the reports.

## Characteristics of Affected Patients

Contrary to earlier reports suggesting that MCRR primarily affects young females[8], our review found that MCRR affects both males and females almost equally, with a slight female predilection at a ratio of 1:1.08. This finding challenges the hypothesis that female hormones are primarily responsible for triggering MCRR. Approximately 53% of the cases occurred in individuals under the age of 30 years, while 25% were discovered in patients over the age of 50 years. Given the asymptomatic nature of MCRR, it is plausible that the disease process began earlier in life but was only detectable later once significant damage or symptoms emerged. Interestingly, cases related to osteoporosis and the use of antiresorptive medications were exclusively observed in postmenopausal women[13,14,24-26,35].

Possible pathways of pathogenesis are summarized in Figure 5.

## Diseases Affecting the Skeletal System

MCRR shares similarities with systemic conditions that affect bone metabolism, as osteoclasts and odontoclasts/cementoclasts, both involved in resorptive processes, are regulated through common signaling pathways[75]. Conditions that increase bone resorption may also predispose teeth to root resorption, especially when the protective cementum layer is compromised. Tooth roots are typically protected from resorption by the precementum and cementoblast layer. However, in certain instances, the cervical region of the root may lack the protective cementum as a developmental anomaly[76]. The protective layer in this region is also prone to damage from occlusal forces, trauma, or chemicals, which can make the cervical region vulnerable to attack from resorptive cells. For example, in osteoporosis, which is prevalent among postmenopausal women, the increased bone loss may be associated with an elevated risk for root resorption. Three MCRR cases were reported in osteoporosis patients who never received antiresorptive medications[24-26]. Liang et al reported another case in an osteopenia patient with elevated parathyroid hormone levels[27].

In addition to osteoporosis, other skeletal diseases with hyperactive osteoclast activity have also been associated with MCRR. Familial expansile osteolysis (FEO) is a rare autosomal dominant genetic disorder characterized by increased bone turnover, middle ear deafness, and dental abnormalities[77]. MCRR was described in FEO patients in 3 reports[19-21]. One of these reports included a large family cohort spanning 5 generations, where 27 out of 42 family members were diagnosed with MCRR[20]. These patients carried mutations in the TNFRSF11 A gene (encoding RANK), leading to heightened RANK-RANKL signaling and increased osteoclast activity, potentially contributing to the resorption process[77].

Gorham-Stout syndrome (GSS) is a rare condition with unknown etiology, involving extensive lymphomatosis and osteolysis[78]. It is also known as the "vanishing bone disease" and is associated with a high rate of morbidity and mortality[79]. Chackartchi et al described a case of MCRR affecting 27 teeth in a patient with GSS[22]. The rate of root resorption appeared to correspond with the overall progression of the disease.

Paget's disease is a relatively common skeletal disorder associated with excessive osteoclast activity[80]. Dental abnormalities such as the cotton wool appearance of the jaw, hypercementosis, and root resorption have been reported in patients with Paget's disease[81,82]. Although apical root resorption is more commonly seen in these patients[83], MCRR can also occur[23].

Furthermore, one report described the occurrence of MCRR in an individual with

**TABLE 1 -** Distribution of Etiologic Factors in Reported MCRR Cases

| Category | Relevant medical/dental history | # Of reports | # Of patients | # Affected teeth |
|---|---|---|---|---|
| Skeletal disorders | Familial expansile osteolysis | 3 | 30 | 181 |
| | Gorham-Stout Syndrome | 1 | 1 | 27 |
| | Paget's disease | 1 | 1 | 4 |
| | Osteoporosis | 3 | 3 | 39 |
| | Osteopenia | 1 | 1 | 8 |
| | Osteogenesis imperfecta | 1 | 1 | 10 |
| Autoimmune diseases | Systemic sclerosis/scleroderma | 4 | 4 | 31 |
| | Celiac disease | 1 | 1 | 6 |
| | Rheumatoid arthritis | 1 | 1 | 3 |
| Liver diseases | Hepatic dysfunction of unknown origin | 1 | 1 | 6 |
| | Hepatitis B | 1 | 1 | 21 |
| Viral infections | Feline herpes | 1 | 4 | 56 |
| | Pertussis virus | 1 | 1 | 6 |
| Medications | Bisphosphonate | 1 | 1 | 5 |
| | Denosumab | 3 | 3 | 46 |
| | Chemotherapy | 1 | 1 | 12 |
| Genetic mutations | Familial pattern | 4 | 5 | 27 |
| | Spontaneous | 2 | 1 | 22 |
| Genetic diseases | Noonan disease | 1 | 1 | 3 |
| | Primary hyperoxaluria | 2 | 2 | 17 |
| | Hereditary hemorrhagic telangiectasia | 1 | 1 | 4 |
| Pregnancy | | 2 | 2 | 37 |
| Other | Inflammatory myofibroblastic tumor | 1 | 1 | 3 |
| | Graft vs host disease | 1 | 1 | 8 |
| Local factors | At home whitening | 1 | 1 | 14 |
| | Malocclusion | 2 | 2 | 18 |
| | Bruxism | 2 | 2 | 15 |
| | Surgery | 1 | 1 | 8 |
| Idiopathic | | 22 | 26 | 284 |
| Total | | 66* | 101 | 921 |

MCRR, multiple cervical root resorption.
*There were 2 reports of multiple cases that belonged to different categories.

osteogenesis imperfecta, which is a rare genetic disorder caused by mutations in type I collagen - a fundamental building block for both bone and teeth[28].

## Antiresorptive Drugs

MCRR has been documented both in patients actively undergoing bisphosphonate and Denosumab therapy[14,36], as well as in those who have discontinued these drugs[13]. Bisphosphonates are widely used for treating osteoporosis and primary or secondary metastatic bone cancers[84]. These drugs effectively prevent bone loss by inhibiting osteoclast formation and function, thereby reducing bone resorption[84]. Denosumab, marketed as Prolia and XGEVA, is a recombinant monoclonal antibody targeting RANKL (receptor activator of nuclear factor kappa B ligand), which is the primary activator of osteoclasts[85]. After a prolonged period of osteoclast inhibition, a rebound effect may occur when patients discontinue Denosumab therapy, leading to hyperactive osteoclasts. This rebound effect has been linked to elevated fracture rates[86] and may also contribute to the development of MCRR. On the other hand, MCRR has also been reported in patients actively receiving antiresorptive therapies. Mikušková reported a case of MCRR in osteoporosis patient who had been on Prolia for 10 years and subsequently developed MCRR in the final 3 years of treatment[14]. This patient also had advanced periodontitis, which may have contributed to the development of MCRR. Another case involved a breast cancer patient treated with Prolia for 7 years[87], during which she developed MCRR affecting 14 teeth in the final 3 years of treatment. Since 2013, 49 cases of root resorption have been reported in patients receiving Prolia, representing a prevalence of 0.03%[88]. However, details on the number of teeth affected and the type of root resorption in these cases are not available. A recent case-control study suggested that Denosumab may be a predictor for ECR;, however, the study lacked detailed information on the duration and status of medication use in affected patients[89]. In addition, the diagnosis of ECR could not be definitively confirmed based on the provided data.

The potential connection between bisphosphonates and root resorption was first proposed by Patel et al in 2015, who suggested that these drugs might influence inflammatory mediators leading to root resorption[35]. However, subsequent studies showed that the elevated levels of IL-1β and TNF-α associated with bisphosphonate treatment were transient and later reversed. In fact, a significant reduction in the number of odontoclasts and odontoclast-mediated root resorption was observed in animal models subjected to orthodontic forces while being treated with bisphosphonates[90].

Osteoclasts and odontoclasts/cementoclasts share common progenitors and differentiation pathways[75]. Their maturation and activation are regulated through complex and overlapping signaling networks, such as the RANK/RANKL/OPG and M-CSF/c-Fms pathways[75]. A plausible explanation of root resorption in patients treated with antiresorptive drugs could be that the inhibition of the RANK/RANKL pathway may lead to a compensatory overactivation of alternative resorptive pathways, which may preferentially act on cementoclasts/osteoclasts lining the root


**FIGURE 4 –** Distribution of etiologic factors in reported MCRR cases. MCRR, multiple cervical root resorption.

surface, leading to increased root resorption. In addition, prolonged inhibition of the RANK/RANKL pathway can result in an accumulation of preclast cells, which may become activated in the presence of inflammatory stimulators such as TNF-α, IL-1, 6, and LPS (lipopolysaccharides). These inflammatory signals can promote osteoclast activity through pathways independent of RANKL[91]. This suggests that chronic inflammation or systemic disease may activate alternative pathways driving cementoclast/osteoclast activation and subsequent root resorption in patients undergoing antiresorptive therapies.

## Autoimmune Diseases

Several autoimmune diseases have been associated with MCRR. SSc has been linked to MCRR in 4 reports[11,29-31]. SSc is a complex autoimmune disease characterized by microvasculature damage, immune system dysfunction, and generalized fibrosis[30]. Patients with SSc often exhibit higher osteoclastic activity[92]. One possible mechanism is that the compression of fibrotic skin over blood vessels leads to impaired blood flow, potentially activating osteoclasts.

MCRR was also reported in a patient with celiac disease, where the diagnosis was made based on elevated antitransglutaminase antibodies levels[32]. The chronic inflammation of the small intestine in Celiac disease can impair the absorption of fat-soluble vitamins, including vitamin D3. Vitamin D3 deficiency may elevate parathyroid hormone levels, which in turn can stimulate osteoclast activity, leading to increased bone and root resorption.

Rheumatoid arthritis is another autoimmune condition associated with MCRR. Rheumatoid arthritis is characterized by chronic systemic inflammation, with elevated levels of pro-inflammatory cytokines such as TNF-α, IL-1β, 2, 6, and GM-CSF[93]. These cytokines may promote the recruitment and activation of cementoclasts in the cervical area of the roots, leading to MCRR.

## Genetics

To date, 6 publications have reported on the genetic analysis of individuals affected by MCRR. Among these, 2 notable studies revealed a familial pattern of MCRR spanning across 2 generations. Neely et al. first described MCRR in a father and son in 2007[41] followed by 2 new cases within the same family involving a daughter and another son, reported in 2015 and 2019[10,42]. Similarly, Muromachi et al reported MCRR in a father and one son in another family[15]. These findings are intriguing as all affected individuals in these studies were otherwise healthy, with no other major contributory systemic diseases.

In these 2 studies, whole-exome sequencing was performed on all family members, comparing the genetic profiles of affected and unaffected individuals to identify

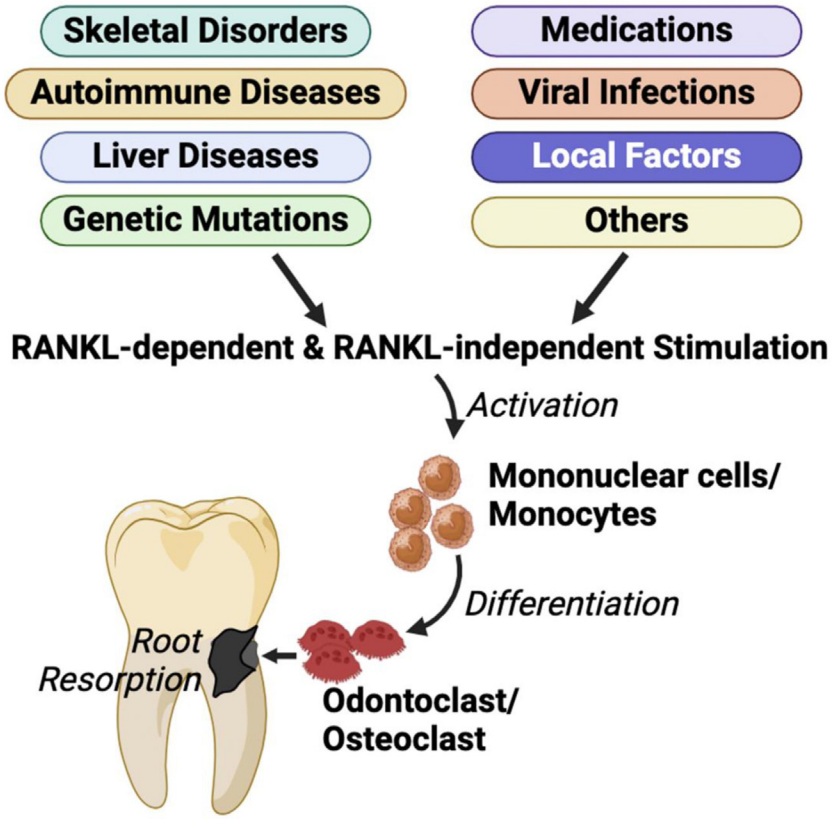


**FIGURE 5 –** A schematic drawing showing the possible pathways of pathogenesis of multiple cervical root resorption.

potential "pathogenic" variants. Neely and Thumbigere-Math's's study identified a missense mutation in the *IRF8* (interferon regulatory factor 8) gene, while Muromachi's study identified a missense mutation in the *DCDC1* (doublecortin domain containing 1) gene. Both genes play crucial roles in inflammation and osteoclast regulation[94,95]. *IRF8* functions as a negative regulator of NFATC1 (Nuclear Factor of Activated T Cells 1), the master regulator of osteoclast differentiation[96]. *IRF8* deficiency results in enhanced osteoclast activity, leading to osteoporosis and root resorption[10,95]. On the other hand, *DCDC1*, is involved in cytokine production and bone metabolism, particularly in the processes of cell fusion and multinucleation, which are essential for osteoclast formation[94]. Interestingly, *IRF8*-associated polymorphisms have been identified as risk factors for other inflammatory diseases, such as systemic lupus erythematosus and multiple sclerosis[97,98]. Decreased levels of *DCDC1* have been reported in patients with Gorham-Stout disease[79], which has also been linked to MCRR[22]. Together, these studies provide strong evidence of genetic components in the etiology of MCRR. *IRF8* and *DCDC1* mutations may serve as screening markers to identify individuals at high risk of MCRR, especially those with a family history of MCRR. As advanced molecular analyses become more readily available, genetic screening of high-risk patients using these markers will become more feasible to allow prevention and early intervention in these patients.

In addition to *IRF8* and *DCDC1*, other gene variants in *DEFB114*[15], *SLC45A2*[15], *FLNA*[16], and *RIT1*[37] have been identified in MCRR affected individuals. Emerging genetic techniques such as CRISPR can be powerful tools to help elucidate the exact roles of specific genes in the resorptive process through selective editing of these genes in animal models.

## Viral Infection

Feline herpes virus-1 (FeHV-1) has been proposed as a possible risk factor for MCRR. A case series involving 4 patients showed a feline connection, where all patients had history of prolonged exposure to domestic cats[12]. Cats commonly carry FeHV-1, which may be transmitted to humans. It is estimated that up to 75% of domestic cats are affected by feline odontoclastic resorptive lesions, which share remarkable similarities with MCRR in humans[99]. Although zoonotic transmission of FeHV-1 has been proposed as a possible cause of MCRR, the exact mechanisms by which this virus may trigger such resorptive lesions in humans remains unclear. Nevertheless, the remarkable parallels between FORL in cats and MCRR in humans underscore the need for further investigation into viral transmission and the pathogenic pathways involved.

Another viral agent linked to MCRR is the herpes zoster virus, particularly when it affects the trigeminal nerve. Herpes zoster, also known as shingles, is known to cause various oral manifestations, including osteonecrosis of the jaw, severe periodontitis, skin and mucosal lesions, and pulpal necrosis. While herpes zoster infection has been associated with root resorption, none of the reported cases involved cervical resorption of more than 3 teeth[100,101]. In 2012, Kjaer et al described a MCRR case that involved multiple teeth on the left side of the jaw, which appeared to cluster along virus-infected nerve paths, presumably related to pertussis[34].

## Genetic Disorders

Several genetic disorders have been implicated in the etiology of MCRR. Primary hyperoxaluria is a rare autosomal recessive disorder characterized by overproduction of oxalate, a metabolic byproduct that leads to the formation of calcium oxalate crystals in various tissues, including the kidneys and periodontal tissues[102]. MCRR has been reported in 2 patients with primary hyperoxaluria[38,39], where the resorption was believed to result from a foreign body reaction in response to calcium oxalate deposits within the periodontal ligament. In such cases, the body's immune response to these deposits could trigger osteoclastic activity, leading to the destruction of the root structures.

Noonan syndrome (NS) is a genetic disorder that affects the overall growth of the cardiac and the skeletal systems. In one patient with NS, sequential loss of mandibular incisors was noted due to MCRR[37]. Although central giant cell lesions in the jaw have been documented in some NS patients, cervical resorption remains rare. The patient in this case report had also undergone orthodontic treatment lasting over 4 years, which may have exacerbated or contributed to the development of MCRR.

Another genetic condition linked to MCRR is hereditary hemorrhagic telangiectasia (HHT), a rare disorder characterized by the development of abnormal blood vessels[103]. In one patient with HHT, MCRR was diagnosed, and histologic analysis of the resorptive defect revealed the presence

of "multiple thin-walled vascular elements as well as large, dilated muscular vessels." This finding suggested a possible causal relationship between the vascular abnormalities in HHT and the development of root resorption. The abnormal blood vessels could lead to compromised blood flow and localized ischemia, which, in turn, might activate osteoclasts and contribute to resorption[40].

### Liver Diseases

The first documented MCRR case was described by Mueller et al in 1930, involving a patient with hepatic dysfunction as the only potential contributing factor[48]. Another case published in 2018, described a healthy individual with MCRR involving 21 teeth, where Hepatitis B was the sole significant medical finding[47]. Chronic liver disease is associated with increased pro-resorptive cytokines, such as IL-1, 6, and TNF-α, which may lead to overactivation of osteoclasts. These cytokines may likely play a role in over-activating osteoclasts/cementoclasts, leading to resorption of the cervical root areas in affected individuals.

### Other Conditions

Malignancies and their treatment have also been linked to MCRR. Merrick et al reported a case of MCRR in a patient with Hopkin's lymphoma who underwent multiple treatment regimens, including chemotherapy, autogenic/allogenic stem cell transplantation. This patient later developed Graft vs Host Disease (GVHD), which was considered to be the most likely cause of MCRR[45]. GVHD, a condition in which donor immune cells attack the host's tissues, leads to widespread inflammation and can exacerbate periodontal destruction, potentially making the roots more vulnerable to resorption.

One of the chemotherapy drugs used early on was bleomycin, which has been associated with another case of MCRR in a patient with ovarian cancer[44]. Bleomycin is known to cause mucosal damage and may also damage the periodontium, including cementum, making the root structure more prone to resorption. However, in one ovarian cancer patient treated with bleomycin, the 7-year gap between drug administration and the onset of MCIR suggests that bleomycin was unlikely to be the primary cause. Instead, the development of GVHD, resulting from the patient's stem cell transplantation, was considered more plausible.

Endocrine dysregulation related to pregnancy[9,49], hormonal treatment[44], or conditions like hyperthyroidism or hyperparathyroidism[10] can induce systemic changes affecting the entire skeletal system, including the teeth, leading to pro-resorptive conditions[91]. Fluctuations in estrogen, progesterone, and testosterone levels can also accelerate tooth movement during orthodontic treatment, increasing the risk of root resorption[104].

### Local Factors

Apart from systemic conditions and medications, local factors can also contribute to the development of MCRR. One case involving 14 teeth reported significant root resorption following the excessive use of 22% carbamide peroxide at-home bleaching[50]. Carbamide peroxide can erode the protective precementum and cementum layers, exposing the underlying dentin to resorptive processes.

Occlusal trauma from bruxism and malocclusion has been implicated in 4 cases[27,52-54], while cleft palate repair surgery was suggested as a possible predisposing factor in another[55]. In these instances, the chemical and mechanical damage to the protective cementum layer in the cervical region was widespread, predisposing multiple teeth to resorption.

Of the 65 published reports, 22 presented no clear contributing medical or dental history, highlighting the importance of conducting a comprehensive evaluation of the patient's medical and dental histories, as well as laboratory tests and imaging studies, to rule out underlying systemic conditions.

Limitations of the current scoping review include the lack of critical appraisal of the included publications due to the absence of any established criteria applicable to case reports. Relying on only case reports is another inherent constraint of this review – the quality of each individual report affects the quality of the review. For example, a lack of identifiable contributing factors could be a result of incomplete review of the patient's medical or dental history, which could lead to an undercount of a potential etiological factor.

## CONCLUSIONS AND CLINICAL IMPLICATIONS

This scoping review provides a comprehensive and up-to-date analysis of published cases of MCRR, highlighting various systemic and local factors contributing to MCRR. Although the precise etiology of MCRR remains elusive, it is clear that systemic diseases associated with bone loss, such as osteoporosis, Paget's disease, FEO, and GSS, as well as medications that affect bone remodeling, play a significant role in a large proportion of cases (40.2%). Additionally, conditions that upregulate the levels of proresorptive cytokines and angiogenesis, such as liver disease, malignancies, and GVHD, may also contribute to many cases of MCRR.

As emphasized by Chu et al in a 2021 article, an interdisciplinary approach is essential for the diagnosis and management of MCRR[105]. It is crucial that general dentists and dental specialists are well-informed of the connections between MCRR and systemic conditions. A thorough review of the patient's medical and dental history, along with the appropriate blood tests and potential genetic testing, can help identify the underlying systemic conditions contributing to MCRR. Likewise, physicians managing systemic diseases linked to MCRR should educate their patients about the importance of regular dental check-ups to enable early detection and management of root resorption. High-risk patients, especially those undergoing orthodontic treatment, antiresorptive therapy, hormone therapy, or cancer treatment, should be closely monitored for early detection and management to minimize the risk of root resorption and tooth loss. Careful consideration should be given to orthodontic treatment and other elective procedures that may increase the risk of root resorption in these patients. The integration of comprehensive medical and dental care is paramount in addressing MCRR, and further research into the mechanisms driving these resorptive processes will help improve diagnostic accuracy and treatment outcomes.

## ACKNOWLEDGMENTS

*The authors deny any conflicts of interest related to this study.*

## REFERENCES


1. Andreasen JO, Andreasen FM. Root resorption following traumatic dental injuries. Proc Finn Dent Soc 1992;88(Suppl 1):95–114.
2. Heithersay GS. Invasive cervical resorption: an analysis of potential predisposing factors. Quintessence Int 1999;30:83–95.
3. Chen Y, Huang Y, Deng X. A review of external cervical resorption. J Endod 2021;47:883–94.
4. Jeng PY, Lin LD, Chang SH, et al. Invasive cervical resorption-distribution, potential predisposing factors, and clinical characteristics. J Endod 2020;46:475–82.
5. Huang J, Walsh RM, Witherspoon DE, et al. The prevalence, characteristics, and risk factors of external cervical resorption: a retrospective practice-based study. Clin Oral Investig 2023;27:5595–604.
6. Nosrat A, Yu P, Verma P, et al. Was the coronavirus disease 2019 pandemic associated with an increased rate of cracked teeth? J Endod 2020;48:1241–7.
7. Machado ICP, Morais MO, Bicalho ALP, et al. Prevalence and characterization of external cervical resorption using cone beam computed tomography. J Endod 2024;50:164–72.
8. Wang N, Zhang M, Zhu J, et al. Multiple idiopathic cervical root resorption: a systematic review. Oral Dis 2023;29:2409–22.
9. Carr G. Multiple idiopathic resorption of teeth. Brit Dent J 1958;105:455–6.
10. Thumbigere-Math V, Foster BL, Bachu M, et al. Inactivating mutation in IRF8 promotes osteoclast transcriptional programs and increases susceptibility to tooth root resorption. J Bone Miner Res 2019;34:1155–68.
11. Matsuda S, Memida T, Mizuno N, et al. Reparative bone-like tissue formation in the tooth of a systemic sclerosis patient. Int Endod J 2018;51:1059–66.
12. von Arx T, Schawalder P, Ackermann M, Bosshardt DD. Human and feline invasive cervical resorptions: the missing link?-presentation of four cases. J Endod 2009;35:904–13.
13. Deeb JG, Azarnoush K, Laskin DM, Deeb GR. Discontinuation of denosumab as a potential cause of generalized external cervical root resorption: a case report. J Endod 2019;45:640–4.
14. Mikuskova K, Vanuga P, Adamicova K, et al. Multiple idiopathic external cervical root resorption in patient treated continuously with denosumab: a case report. BMC Oral Health 2022;22:129.
15. Muromachi K, Hosomichi K, Park H, et al. Identification of candidate genes of familial multiple idiopathic cervical root resorption. J Endod 2023;49:1537–47.
16. Qin W, Gao J, Ma S, et al. Multiple cervical root resorption involving 22 teeth: a case with potential genetic predisposition. J Endod 2022;48:1526–32.
17. Heithersay GS. Invasive cervical resorption. Endod Top 2004;7:73–92.
18. Munn Z, Peters MDJ, Stern C, et al. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018;18:143.
19. Macaraeg K, Lee SM, Kalra L, et al. Multiple external root resorption in a pediatric patient with familial expansile osteolysis. Pediatr Dent 2020;42:62–5.
20. Mitchell CA, Kennedy JG, Wallace RG. Dental abnormalities associated with familial expansile osteolysis: a clinical and radiographic study. Oral Surg Oral Med Oral Pathol 1990;70:301–7.
21. Olsen CB, Tangchaitrong K, Chippendale I, et al. Tooth root resorption associated with a familial bone dysplasia affecting mother and daughter. Pediatr Dent 1999;21:363–7.
22. Chackartchi T, G T, J M, M F. Dental resorption in gorham-stout syndrome. Arch Clin Med Case Rep 2022;6:521–3.
23. Smith NH. Monostotic paget's disease of the mandible presenting with progressive resorption of the teeth. Oral Surg Oral Med Oral Pathol Oral 1978;46:246–53.
24. Iwamatsu-Kobayashi Y, Satoh-Kuriwada S, Yamamoto T, et al. A case of multiple idiopathic external root resorption: a 6-year follow-up study. Oral Surg Oral Med Oral Pathol 2005;100:772–9.
25. Kerr DA, Courtney RM, Burkes EJ. Multiple idiopathic root resorption. Oral Surg Oral Med Oral Pathol 1970;29:552.

26. Konishi RMA, Yoshida T. A case of multiple idiopathic root resorption. Open J Stomatol 2023;13:156–65.

27. Liang H, Burkes EJ, Frederiksen NL. Multiple idiopathic cervical root resorption: systematic review and report of four cases. Dentomaxillofac Radiol 2003;32:150–5.

28. Thoma KH, Sosman MC, Bennett GA. An unusual case of hereditary fibrous osteodysplasia (fragilitas ossium) with replacement of dentin by osteocementum. Am J Orthod Oral Surg 1943;29.

29. Arroyo-Bote S, Bucchi C, Manzanares MC. External cervical resorption: a new oral manifestation of systemic sclerosis. J Endod 2017;43:1740–3.

30. Elmatary A, Longridge N, Jarad F. Is external cervical resorption an established manifestation of systemic sclerosis? A case report. J Endod 2023;49:915–9.

31. Journo JE, Woodmansey KF, Walsh RM. Scleroderma and multiple teeth with invasive cervical resorption: is there a connection? Gen Dent 2022;70:41–4.

32. Dobros K, Mycinski P, Borowy P, Zarzecka J. Multiple invasive cervical resorption and celiac disease: a case report. Quintessence int 2018;49:407–12.

33. Jabali AH. Management of multiple idiopathic root resorption in a rheumatoid arthritis patient: a case report with 4-year follow-up. J Contemp Dent Pract 2022;23:652–8.

34. Kjaer I, Strom C, Worsaae N. Regional aggressive root resorption caused by neuronal virus infection. Case Rep Dent 2012;2012:693240.

35. Patel S, Saberi N. External cervical resorption associated with the use of bisphosphonates: a case series. J Endod 2015;41:742–8.

36. Beaumont S, Angel CM, Dawson SJ. Denosumab and invasive cervical root resorption: a case report. Aust Dent J 2022;67:183–9.

37. Friedrich RE, Scheuer HA. Sequential loss of mandibular permanent incisors in noonan syndrome. In Vivo (Athens) 2022;36:1021–9.

38. Moskow BS. Periodontal manifestations of hyperoxaluria and oxalosis. J Periodontol 1989;60:271–8.

39. Wysocki GP, Fay WP, Ulrichsen RF, Ulan RA. Oral findings in primary hyperoxaluria and oxalosis. Oral Surg Oral Med Oral Pathol 1982;53:267–72.

40. Edwards PC, McVaney T. External cervical root resorption involving multiple maxillary teeth in a patient with hereditary hemorrhagic telangiectasia. Oral Surg Oral Med Oral Pathol 2005;100:585–91.

41. Neely AL, Gordon SC. A familial pattern of multiple idiopathic cervical root resorption in a father and son: a 22-year follow-up. J Periodontol 2007;78:367–71.

42. Neely AL, Thumbigere-Math V, Somerman MJ, Foster BLA. Familial pattern of multiple idiopathic cervical root resorption with a 30-year follow-up. J Periodontol 2016;87:426–33.

43. Wang YM, Ruan WY, Chi DD, Duan XH. Clinical and genetic analysis of multiple idiopathic cervical root resorption. Chin J Dent Res 2024;27:89–99.

44. Llavayol M, Pons M, Lluisa Ballester M, Berastegui E. Multiple cervical root resorption in a young adult female previously treated with chemotherapy: a case report. J Endod 2019;45:349–53.

45. Merrick D, Duncan HF, Bolas A, et al. Multiple external cervical resorption lesions in patient with graft versus host disease treated with systemic bleomycin: a case report. J Endod 2024;50:674–9.

46. Rautava J, Soukka T, Peltonen E, et al. Unusual case of inflammatory myofibroblastic tumor in maxilla. Case Rep Dent 2013;2013:876503.

47. Kumar V, Chawla A, Kaur A. Multiple idiopathic cervical root resorptions in patients with hepatitis B virus infection. J Endod 2018;44:1575–7.

48. Mueller E, Rony HR. Laboratory studies of an unusual case of resorption. J Am Dent Assoc 1930;17:326–34.

49. Chen X, Yu X, Yan K, et al. Multiple idiopathic cervical root resorption involving all permanent teeth. Aust Endod J 2020;46:263–71.

50. Velloso GR, de Freitas MM, Alves A, et al. Multiple external cervical root resorptions after home whitening treatment: a case report. Aust Dent J 2017;62:528–33.

51. George DI, Miller RL. Idiopathic resorption of teeth a report of three cases. Am J Orthod 1986;89:13–20.

52. Nikolidakis D, Nikou G, Meijer GJ, Jansen JA. Cervical external root resorption: 3-year follow-up of a case. J Oral Sci 2008;50:487–91.

53. Mattar R, de Lima Pereira SA, Rodor RC, Rodrigues DBR. External multiple invasive cervical resorption with subsequent arrest of the resorption. Dent Traumatol 2008;24:556–9.

54. Samara E, Kelly E, Walker R, Borumandi F. Multiple idiopathic cervical root resorption: case report of an unusual presentation. Spec Care Dentist 2021;41:98–102.

55. Coyle M, Toner M, Barry H. Multiple teeth showing invasive cervical resorption–an entity with little known histologic features. J Oral Pathol Med 2006;35:55–7.

56. Ali R, Fayle S, Langley D, et al. Dental management of a patient with multiple idiopathic cervical root resorption. Dent Update 2015;42:667–8.

57. Arora A, Acharya SR, Muliya VS, Sharma P. Multiple idiopathic cervical resorption: a diagnostic dilemma. Quintessence Int 2012;43:187–90.

58. Beckett HA, Gilmour AG. Multiple idiopathic cervical root resorption in a male. Br Dent J 1993;175:33–4.

59. Sharma S, Kumar P, Jain V, Logani A. Multiple idiopathic cervical root resorption: diagnosis, clinical/radiographical/histological presentation, and rehabilitation - a 7-year follow-up case report. J Conserv Dent 2019;22:313–7.

60. Shashidara R, Sudheendra US, Aparna HG, Kavita AP. Multiple idiopathic cervical resorption a case report. J Multidiscip Dent Res 2018;4:34–8.

61. Choudhury P, Panigrahi RG, Maragathavalli PA, Patra PC. Vanishing roots: first case report of idiopathic multiple cervico-apical external root resorption. J Clin Diagnostic Res 2015;9:ZD17–9.

62. Haeberle CB. Prosthodontic rehabilitation of a patient diagnosed with multiple idiopathic root resorption. J Prosthet Dent 2013;110:442–6.

63. Hata H, Abe M, Mayanagi H. Multiple lesions of intracoronal resorption of permanent teeth in the developing dentition: a case report. Pediatr Dent 2007;29:420–5.

64. Jiang Y-H, Lin Y, Ge J, et al. Multiple idiopathic cervical root resorptions: report of one case with 8 teeth involved successively. Int J Clin Exp Med 2014;7:1155–9.

65. Kesary SR, Mengji A, Yaga U, Panta P. An unusual case of idiopathic multiple invasive cervical resorption. J Indian Acad Oral Med Radiol 2014;26:229–32.

66. Roy DK, Sharma S, Suwal P, et al. Multiple idiopathic cervical resorption: a case report. Bangladesh J Med Sci 2012;11:151–3.

67. Wu J, Lin LY, Yang J, et al. Multiple idiopathic cervical root resorption: a case report. Int Endod J 2016;49:189–202.

68. Hopkins R, Adams D. Multiple idiopathic resorption of the teeth. Br Dent J 1979;146:309–12.

69. Moody AB, Speculand B, Smith AJ, Basu MK. Multiple idiopathic external resorption of teeth. Int J Oral Maxillofac Surg 1990;19:200–2.

70. Moody GH, Muir KF. Multiple idiopathic root resorption - a case-report and discussion of pathogenesis. J Clin Periodontol 1991;18:577–80.

71. Yu VSH, Messer HH, Tan KB. Multiple idiopathic cervical resorption: case report and discussion of management options. Int Endod J 2011;44:77–85.

72. Jensen JL, Solheim T, Koppang HS, Arvidsson LZ. Aggressive external root resorption of the entire dentition accompanied by osteolysis: a case report. Int J Prosthod 2012;25:459–64.

73. Lydiatt DD, Hollins RR, Peterson G. Multiple idiopathic root resorption - diagnostic considerations. Oral Surg Oral Med Oral Pathol 1989;67:208–10.

74. Yilmaz B, Diker E, Ovchinnik V, Abou-Ayash S. Management of a partially edentulous patient with idiopathic root resorption by using digital and conventional implant planning technologies. J Prosthet Dent 2022;127:15–21.

75. Wang Z, McCauley LK. Osteoclasts and odontoclasts: signaling pathways to development and disease. Oral Dis 2011;17:129–42.

76. Neuvald L, Consolaro A. Cementoenamel junction: microscopic analysis and external cervical resorption. J Endod 2000;26:503–8.

77. Hughes AE, Ralston SH, Marken J, et al. Mutations in TNFRSF11A, affecting the signal peptide of RANK, cause familial expansile osteolysis. Nat Genet 2000;24:45–8.

78. Gondivkar SM, Gadbail AR. Gorham-stout syndrome: a rare clinical entity and review of literature. Oral Surg Oral Med Oral Pathol 2010;109:e41–8.

79. Rossi M, Buonuomo PS, Battafarano G, et al. Dissecting the mechanisms of bone loss in Gorham-Stout disease. Bone 2020;130:115068.

80. Kravets I. Paget's disease of bone: diagnosis and treatment. Am J Med 2018;131:1298–303.

81. Smith BJ, Eveson JW. Paget's disease of bone with particular reference to dentistry. J Oral Pathol 1981;10:233–47.

82. Helfrich MH. Osteoclast diseases and dental abnormalities. Arch Oral Bio 2005;150:115–22.

83. Barnett F, Elfenbein L. Paget's disease of the mandible–a review and report of a case. Endod Dent Traumatol 1985;1:39–42.

84. Drake MT, Clarke BL, Khosla S. Bisphosphonates: mechanism of action and role in clinical practice. Mayo Clin Proc 2008;83:1032–45.

85. Hanley DA, Adachi JD, Bell A, Brown V. Denosumab: mechanism of action and clinical outcomes. Int J Clin Pract 2012;66:1139–46.

86. Eastell R, Christiansen C, Grauer A, et al. Effects of denosumab on bone turnover markers in postmenopausal osteoporosis. J Bone Miner Res 2011;26:530–7.

87. Beaumont denosumab and invasive cervical root resorption: a case report. Aust Dent J 2022;67:183–9.

88. Prolia and Tooth resorption - a phase IV clinical study of FDA data. Available at: https://www.ehealthme.com/ds/prolia/tooth-resorption/. [Accessed 15 October 2024].

89. Alyahya L, Myers GL. Denosumab use as a predictor variable for external cervical resorption: a case-control study. J Endod 2021;47:366–73.

90. Rama Putranto YO, Kaneko K, Shioyasono A, Moriyama K. Effects of bisphosphonates on root resorption and cytokine expression during experimental tooth movement in rats. Orthod Waves 2008;67:141–9.

91. Feng W, Guo J, Li M. RANKL-Independent modulation of osteoclastogenesis. J Oral Biosci 2019;61:16–21.

92. Park JK, Fava A, Carrino J, et al. Association of acroosteolysis with enhanced osteoclastogenesis and higher blood levels of vascular endothelial growth factor in systemic sclerosis. Arthritis Rheumatol 2016;68:201–9.

93. Kondo N, Kuroda T, Kobayashi D. Cytokine networks in the pathogenesis of rheumatoid arthritis. Int J Mol Sci 2021;22:10922.

94. Kaplan A, Reiner O. Linking cytoplasmic dynein and transport of Rab8 vesicles to the midbody during cytokinesis by the doublecortin domain-containing 5 protein. J Cell Sci 2011;124:3989–4000.

95. Zhao B, Takami M, Yamada A, et al. Interferon regulatory factor-8 regulates bone metabolism by suppressing osteoclastogenesis. Nat Med 2009;15:1066–71.

96. Yao Z, Getting SJ, Locke IC. Regulation of TNF-induced osteoclast differentiation. Cells 2021;11:132.

97. Cunninghame Graham DS, Morris DL, Bhangale TR, et al. Association of NCF2, IKZF1, IRF8, IFIH1, and TYK2 with systemic lupus erythematosus. PLoS Genet 2011;7:e1002341.

98. De Jager PL, Jia X, Wang J, et al. Meta-analysis of genome scans and replication identify CD6, IRF8 and TNFRSF1A as new multiple sclerosis susceptibility loci. Nat Genet 2009;41:776–82. https://doi.org/10.1038/ng.401.

99. Lommer MJ, Verstraete FJ. Prevalence of odontoclastic resorption lesions and periapical radiographic lucencies in cats: 265 cases (1995-1998). J Am Vet Med Assoc 2000;217:1866–9.

100. Solomon CS, Coffiner MO, Chalfin HE. Herpes zoster revisited: implicated in root resorption. J Endod 1986;12:210–3.

101. Ramchandani PL, Mellor TK. Herpes zoster associated with tooth resorption and periapical lesions. Br J Oral Maxillofac Surg 2007;45:71–3.

102. Mitsimponas KT, Wehrhan T, Falk S, et al. Oral findings associated with primary hyperoxaluria type I. J Craniomaxillofac Surg 2012;40:e301–6.

103. Viteri-Noël A, González-García A, Patier JL, et al. Hereditary hemorrhagic telangiectasia: genetics, pathophysiology, diagnosis, and management. J Clin Med 2022;11:5245.

104. Deng L, Guo Y. Estrogen effects on orthodontic tooth movement and orthodontically-induced root resorption. Arch Oral Biol 2020;118:104840.

105. Chu EY, Deeb JG, Foster BL, et al. Multiple idiopathic cervical root resorption: a challenge for a transdisciplinary medical-dental team. Front Dent Med 2021;2:652605.