



Non- Syndromic Multiple Dentigerous Cyst in Indian Population: A Systematic Review

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KEYWORDS

Odontogenic cyst, surgical enucleation

ABSTRACT:

Introduction: Odontogenic cysts are epithelial lined pathologic cavities surrounded by fibrous connective tissue originating from the odontogenic apparatus. Dentigerous cyst is the 2nd most common type of odontogenic cyst and can present as solitary or multiple lesions. While multiple dentigerous cysts are commonly associated with syndromic conditions such as Mucopolysaccharidosis type VI and Gardner's syndrome, their occurrence in non-syndromic cases has also been reported, although it remains relatively underexplored in the literature.

Objectives: The objective of this systematic review is to explore the demographics, etiopathogenesis, treatment and prognosis of Non -syndromic multiple dentigerous cysts (NSMDCs).

Methods: Search strategy was implemented from the year 2004- 2025 (April) involving Indian population. Various databases were searched based upon the defined selection criteria. Risk of bias assessment was done using the JBI critical appraisal tool.

Results: The final 32 cases were selected. The observed age, gender and site predilections were consistent with those typically associated with dentigerous cyst. There was no reported recurrence for a period of upto 1 year and the prognosis of the lesion was good.

Conclusions: The cases of NSMDCs have gradually increased over the period of time. However, there exists a significant knowledge gap regarding its true nature and etiopathogenesis, primarily due to the limited number of reported cases. Comprehensive case documentation, including detailed medical and family history, along with thorough clinical, radiographic, and histopathological investigations, is essential to enhance our knowledge regarding this entity.

1. Introduction

Cysts of oral and maxillofacial region are common and constitute about 20% of all lesions encountered in oral and maxillofacial pathologies [1]. Cysts of jaws are divided into two major categories depending upon its relationship with odontogenic apparatus: Odontogenic cyst (OC) and Non- odontogenic cyst. OCs have further been subdivided into inflammatory and developmental type. Dentigerous cyst (DC) is a subtype of OC; which is the second most common type of OC and most common developmental OC (24%) [2]. According to Browne (1991b), DC is a cyst which encloses the crown of an unerupted tooth lying within the bone and can not be

assigned to any other classification [1]. Their frequency in the general population has been estimated to be 1.44 cyst for every 100 unerupted teeth [2]; therefore, it needs to be studied extensively.

DCs can present as solitary or multiple lesions. Although mostly multiple DCs occur in association with syndromes like Cleidocranial dysplasia, Nevroid BCC syndrome, Gardner's syndrome & Maroteaux Lamy syndrome (Mucopolysaccharidosis type VI); multiple DCs in non-syndromic cases are extremely rare (1.8-3%) [3].

The "key event" in the etiopathogenesis of DC is accumulation of pathological fluid in the layer of the



reduced enamel epithelium (REE) or between it and the crown of an un-erupted tooth; however, the plausible etiopathogenesis of NSMDC include:

1. Subtle genetic mutations or familial tendencies which are not classified as syndromes:

Batra P reported Chromosomal polymorphism in bilateral dentigerous cyst whose karyotyping revealed a large secondary constriction in one of the chromosome 1 pair (1qh+) [4]. Studying the chromosomal analysis may lead to the discovery of new or subclinical genetic associations.

2. Drug induced gingival overgrowth (DIGO):

Some authors have studied the relationship between gingival overgrowth and HLA phenotype. A possible protective effect exerted by HLA-B37 and the elevated risk associated with HLA-DR2 has been described [5].

Table 1: Drugs inducing gingival overgrowth and their mechanism of action.

Drug class	Mean duration of onset	Mechanism of action
Immunosuppressants	71 days	Blocks cytosolic protein – cyclophilin
Anticonvulsants	37 days	Blocks sodium channels
Ca channel blockers	262 days	Blocks Calcium channels

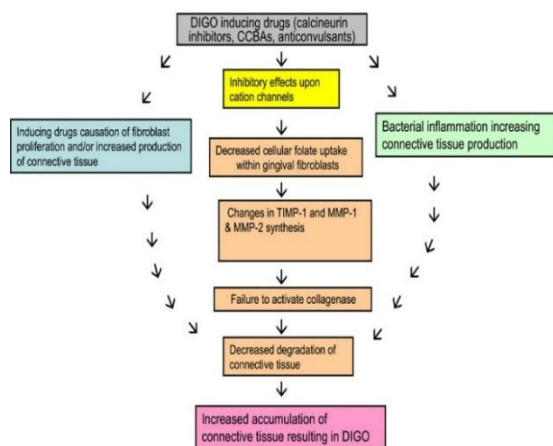


Fig 1: Mechanism of DIGO [5]

Although DCs show a peak incidence in the 3rd and 4th decades, NSMDCs are more common in children and adults. Understanding their presentation helps clinicians differentiate non-syndromic cases from those requiring broader systemic investigation. Syndromic cases may require multidisciplinary management due to systemic involvement. Non-syndromic multiple Dentigerous cysts (NSMDCs) in contrast, can often be managed with localized surgical intervention i.e., enucleation or marsupialization. Recognizing the distinction prevents over-investigation or under-treatment. Reporting and studying these rare cases contribute to the global and regional epidemiological data, especially in under-reported populations like in India.

Objectives

The objective of this systematic review is to explore the demographics, etiopathogenesis, treatment and prognosis of Non -syndromic multiple dentigerous cysts (NSMDCs) in Indian population.

Methods

Protocol development: The search protocol is designed based on the PRISMA (Preferred reporting items for systematic reviews and meta-analysis) guidelines 2020 statement and PROSPERO registration was done-CRD42025639175.

Study design: The focused research question was proposed in the following format “Is there any difference in the demographics, etiopathogenesis, histopathology, treatment and prognosis of Dentigerous cyst compared to Non - syndromic multiple Dentigerous cysts in Indian population?”

Eligibility criteria:

Inclusion criteria:

- 1) Case report & case series published in English language.
- 2) Case report and case series published in open access journals between January 2000 and April 2025.
- 3) Case report and case series that investigated patients with Non syndromic multiple Dentigerous cysts in the Indian population and had relevant data on demographic details and the age, gender, site, size, clinical appearance,



symptoms, histopathological diagnosis, treatment & follow-up of the patient.

2. Exclusion criteria:

- 1) Case report & case series that did not use histopathology as the reference for standard diagnosis.
- 2) Book chapters, conference abstracts, letters, personal opinions, reviews.
- 3) Case report & case series of dentigerous cyst along with any other pathology.

Table 2: Search strategy according to PECOS

Component	Search terms (MeSH + Free Text)
Population	("dentigerous cyst" [MeSH] OR "dentigerous cysts" OR "odontogenic cyst" [MeSH])
Exposure	("multiple dentigerous cyst" OR "bilateral dentigerous cyst") AND ("non- syndromic")
Comparison	("solitary dentigerous cyst")
Outcome	("clinical features" OR "radiographic features" OR "histopathologic features" OR "etiopathogenesis" OR "treatment" OR "management" OR "recurrence")
Study design	("case reports" OR "case series")

Search strategy:

For the research published within the last 25 years (from 2000 to April 2025), an electronic data search was carried out by two independent reviewers. Various databases including MEDLINE (Ovid), PubMed, SCOPUS, Science Citation Index Expanded (SCIEXPANDED), Google Scholar, BU Library search, LILACS, LIVIVO using proper keywords with Boolean operators like AND/ OR (Table 2).

Screening process:

A rigorous two- phase screening process was conducted by two independent authors to select relevant articles. Initially, titles and abstracts were reviewed, and non-relevant articles were excluded. In phase two, full- text reviews were performed independently by the same reviewers, with disputes resolved through discussions. A

third reviewer was consulted when necessary to ensure consensus.

Data extraction:

For all included studies, the study details were extracted under the following headings: Author(s), year of study, parameters accessed and conclusion.

Evaluation of risk of bias

Risk of bias assessment was done by two independent reviewers used Joanna Briggs Institute (JBI) critical appraisal tool for the quality appraisal.

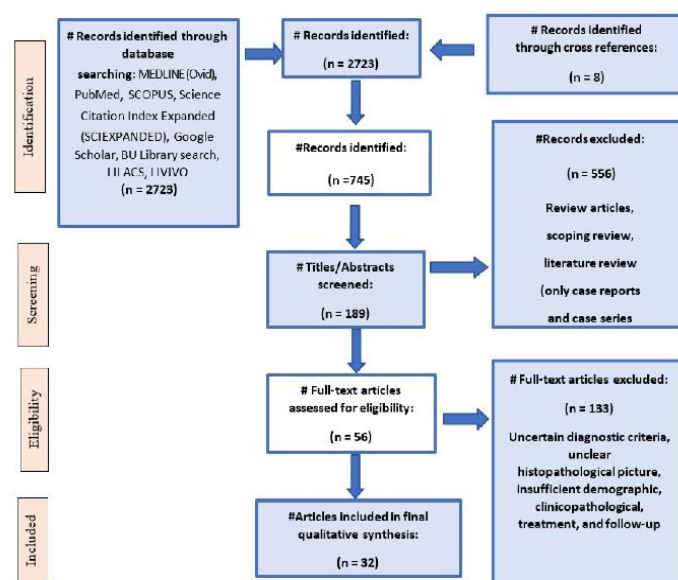


Figure 2: PRISMA 2020 flowchart

Results

Study characteristics

As shown in table 3, data were evaluated from 32 studies from an aggregate of a total sample of 2732.

Risk of bias assessment

- 15 studies revealed a 'low risk of bias' (studies: 1,3,5,7,8,12,13,17,18,20,21,22,26,29,31)
- 17 studies presented with a 'moderate risk of bias' (studies:2,4,6,9,10,11,14,15,16,19,23,24,25,27,28,30,32)

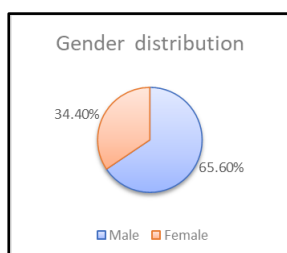


Figure 3: Pie chart showing the gender distribution among NSMDCs

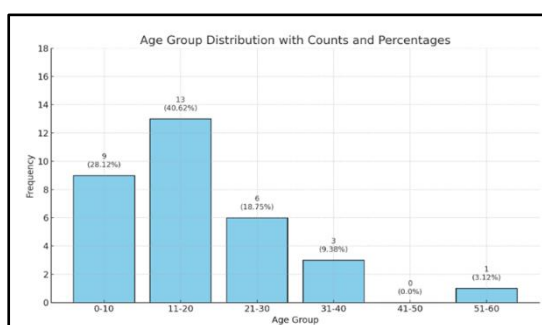


Figure 4: Bar graph showing age distribution among NSMDCs

Discussion

Dentigerous cysts (DCs) encompass the 2nd most common odontogenic cyst, followed by Radicular cyst. These may present as solitary lesions or, less commonly, as multiple cysts, particularly in cases of syndromes like Cleidocranial dysplasia, Maroteaux–Lamy syndrome and Mucopolysaccharidosis VI. However, secondarily infected DCs are also found to be associated with rare clinical entities such as Orbital Apex Syndrome and Superior Orbital Fissure Syndrome, typically arising from cysts located in the maxillary or adjacent regions [13].

Alternatively, multiple DCs in non- syndromic cases are also seen. In this systematic review, we reported 32 cases of NSMDCs out of which 65.6% (n= 21) were males and 34.4% (n=11) were females. The mean age of patients was 17.9 years (range= 9-51 years). The most frequently involved site was bilateral mandible (n=13) > bilateral maxilla (n=9) > bilateral maxilla with bilateral mandible (n=3). Jeon et al [43] also reported a case where bilateral involvement of maxilla and mandible was noted. However, other combinations are also available in the

literature. 71.8% (n=23) cases were symptomatic and 28.2% (n=9) were asymptomatic. Yamalik K et al [44] highlighted the potential synergistic effect of cyclosporine and calcium channel blockers in the pathogenesis of bilateral dentigerous cysts. Although, genetic variability is mostly seen in association with syndromes, subtle genetic mutations can be possible for the occurrence of multiple dentigerous cysts. Batra et al. [12] reported a case with polymorphism in chromosome 1qh+. Moutri et al [11] highlighted the potential role of antiepileptic medicines in contributing to gingival hypertrophy. This is also supported by authors Isike De Biase A et al [9] who reported that prolonged concomitant administration of cyclosporine A and calcium channel blockers may contribute to the development of bilateral mandibular dentigerous cysts. This drug-induced gingival overgrowth can act as a mechanical barrier, thereby obstructing the normal path of tooth eruption. Adnan et al reported a case suggestive of familial predisposition [39]. These observations imply that factors such as antiepileptic medication, diabetes mellitus, and genetic background may serve as potential predisposing conditions in the pathogenesis of NSMDCs. However, in approximately 32% of reported cases, relevant medical history was not provided. This highlights the importance of thorough documentation of family and medical history in order to facilitate a more comprehensive understanding of their etiologies.

Radiographic findings from this systematic review revealed multiple unilocular radiolucencies having sclerotic border and associated with crown of unerupted or impacted teeth. CT or Cone beam computed tomography are proved to be useful than OPG, as they provide superior details of the hard tissues [19]. Differential diagnosis of multiple jaw cysts include-odontogenic keratocyst and unicystic ameloblastoma, radicular cysts, periapical cysts, infected dental cysts, and other odontogenic lesions [10].

Therefore, histopathological evaluation is essential for definitive diagnosis. Although a typical DC is uninfamed, areas of inflammation are seen in secondarily infected cases [1]. Histopathological evaluation shows presence of 2-4 cell layers of non-keratinized stratified squamous epithelium resembling REE. Abundance of chronic inflammatory cellular



components were also seen which coincides with high frequency of symptomatic cases (71.8%).

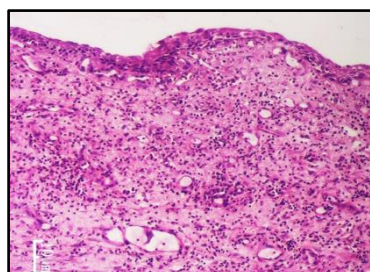


Fig. 5: The wall of a DC showing a typical lining of 2 - 4 cell layers of non-keratinized stratified squamous epithelium.

DC, however benign, is potentially capable of undergoing transformation into neoplasms like Adenomatoid Odontogenic Tumor, Complex odontoma, Ameloblastoma, Primary intraosseous squamous cell carcinoma, Mucoepidermoid carcinoma and Unicystic ameloblastoma. Surgical management of NSMDCs include either enucleation or marsupialization. However, the treatment of choice is enucleation along with extraction of the impacted tooth, marsupialization has to be considered to save the impacted tooth and developing tooth bud, specially in pediatric patients. Therefore, the ideal choice of treatment depends upon age of the patient's age, type of dentition, location of cyst along with offending tooth, inclination and position of impacted tooth and root formation [42]. There has been no reported recurrence and the prognosis of the disease is good.

Conclusion

Non-syndromic multiple dentigerous cysts (NSMDCs) are rare odontogenic lesions, with only a limited number of cases documented in the Indian population. The observed age, gender, and site predilections were consistent with those typically associated with solitary DCs. As awareness and documentation of these cases will improve, an increase in reported cases is expected. This review also underscores the potential involvement of drug-induced gingival overgrowth (DIGO), chromosomal abnormalities and familial predisposition in the etiopathogenesis of NSMDCs.

Further research and comprehensive case reports are

necessary to enhance the understanding regarding etiopathogenesis and thereby establishing the standardized clinical, radiographic, and histopathological criteria for accurate diagnosis and effective management of NSMDCs.

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