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Clinical, radiographic, and histological features of buccal bifurcation cysts: A systematic review to aid accurate diagnosis and treatment decisions

Matheus de Castro Costa [a], Rani Kanthan [b], Marina Lara de Carli [c], Felipe Fornias Sperandio [d,*]

[a] Bauru School of Dentistry, University of São Paulo, Alameda Dr. Octávio Pinheiro Brisolla, Quadra 9 - Jardim Brasil, Bauru, SP, 17012-901, Brazil
[b] Dept. of Pathology and Laboratory Medicine, College of Medicine, University of Saskatchewan, 103 Hospital Dr, Saskatoon, SK, S7N 0W8, Saskatoon, Canada
[c] College of Dentistry, Federal University of Alfenas, Rua Gabriel Monteiro da Silva 700, Alfenas, MG, 37130-001, Brazil
[d] College of Dentistry, University of Saskatchewan, 105 Wiggins Road, Saskatoon, SK, S7N 5E4, Canada

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ABSTRACT

Objective: This systematic review delves into the nuanced landscape of buccal bifurcation cysts (BBCs), emphasizing their clinical significance amid the diagnostic challenges in oral and maxillofacial pathology. We trace the evolution of BBC classification from historical perspectives to its current status in the World Health Organization's classification system, aiming to equip dental professionals with crucial insights for accurate diagnosis and effective management.

Methods: This systematic review (PROSPERO: CRD42023405169) followed PRISMA guidelines to examine the epidemiological characteristics of BBCs. Observational studies were included, while reviews, meta-analyses, and experimental studies were excluded. A comprehensive search across five databases identified eligible studies. Two independent reviewers screened articles, resolving disagreements by consensus or a third reviewer. Data extraction included clinical, histological, and imaging findings. Risk of bias was assessed using Murad's framework for case reports/series and the Newcastle–Ottawa Scale for other study types, with studies rated as low, moderate, or high quality.

Results: The information presented here is crucial for preventing past treatment errors associated with BBC. In addition, this review confirms that BBCs predominantly affect the posterior mandible of pediatric patients and exhibit consistent clinical and histopathological features, aiding in their differentiation from similar maxillofacial lesions. Thus, well-informed clinicians should be able to diagnose BBC and make a proper treatment choice after familiarizing themselves with this review, which will ultimately lead to a favorable prognostic outcome and reduced risk of lesion recurrence.

Conclusion: This study provides a comprehensive analysis of BBC, aiming to enhance clinical understanding and ultimately improve patient care.

1. Introduction

The landscape of oral and maxillofacial pathology is rich with entities that present diagnostic and therapeutic challenges to clinicians. Among these, the buccal bifurcation cyst (BBC) stands out as a clinically significant lesion due to its distinctive characteristics and its potential for misdiagnosis. Over the years, the classification and understanding of BBC have evolved, reflecting advancements in our comprehension of its etiology, histopathological features, and management strategies.

Historical perspectives reveal a trajectory marked by changing nomenclature and evolving conceptual frameworks surrounding this 'BBC'. Initially described in 1983 as the mandibular infected buccal cyst-molar area, BBC was later referred to by various terms including circumferential dentigerous cyst, inflammatory collateral cyst (ICC), mandibular infected cyst (MIC), inflammatory lateral periodontal cyst, and paradental cyst [1–8]. This terminological variation has led to inconsistencies, making it difficult to accurately interpret epidemiological data due to misdiagnosis. Each designation attempts to capture the anatomical location and unique association of the lesion with the mandibular first and second molars. For instance, the term "mandibular

* Corresponding author. College of Dentistry, University of Saskatchewan, 105 Wiggins Road, Saskatoon, SK, S7N 5E4, Canada.
E-mail address: felipe.sperandio@usask.ca (F.F. Sperandio).

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buccal bifurcation cyst" was introduced to more precisely describe its location [3].

Understanding the nomenclature surrounding BBC is essential when reviewing past literature to ensure a proper final diagnosis was reached in these publications. Specifically, ICCs are inflammatory cysts located on the buccal or distobuccal aspect of the roots of partially or recently erupted teeth. This term encompasses both BBCs and paradental cysts, the latter being similarly associated with partially erupted molars. However, paradental cysts typically occur more frequently on the distal aspect of third molars, differently than showing buccal surface location or a relationship with the buccal bifurcation, which is a key feature of BBC [3]. Additionally, BBCs may have been misdiagnosed as lateral radicular cysts [9,10], as they can share similar radiographic features. However, clinical aspects such as tooth vitality testing should aid in differentiating these cysts. This underscores the importance of thorough clinical and radiological evaluation in accurately diagnosing BBCs and distinguishing them from other inflammatory and developmental odontogenic cysts, including lateral periodontal cysts and odontogenic keratocysts (OKC) [11].

Classification systems, notably the World Health Organization (WHO) classification of odontogenic tumors and cysts, have played a pivotal role in shaping our understanding of BBC. Designated as an inflammatory odontogenic cyst in the 1992 WHO classification, BBC's classification as an inflammatory odontogenic cyst remains unchanged in subsequent editions [4]. This classification underscores the inflammatory nature of the lesion and its distinct histopathological features compared to other odontogenic cysts, positioning BBC within the spectrum of inflammatory collateral cysts alongside paradental cysts.

Etiologically, BBC is linked to inflammation in the pericoronal tissues, often exacerbated by factors such as food impaction or the presence of enamel projections on the buccal aspect of the affected tooth. Pathogenetically, BBCs are characterized as "pocket" cysts resulting from dilation of the pericoronal tissues, with sulcular or junctional epithelium lining the cystic cavity [12–14]. This etiological and pathogenetic understanding underscores the unique diagnostic criteria for BBC, distinguishing it from radicular cysts and dentigerous cysts.

Epidemiologically, BBCs exhibit distinct demographic patterns, with a predilection for occurrence in pediatric patients, particularly in the posterior mandible [12,15]. Clinical manifestations commonly include signs of infection such as pain, tenderness, and suppuration, highlighting the importance of accurate diagnosis and timely intervention. Radiographically, BBCs present as corticated radiolucencies over the buccal or distobuccal region of the affected tooth, often accompanied by deep periodontal pockets, necessitating careful radiological evaluation for differential diagnosis.

Histopathologically, BBCs exhibit consistent features characterized by non-keratinized stratified squamous epithelium with varying degrees of hyperplasia, accompanied by a chronic inflammatory infiltrate within the connective tissue wall. Despite variations in descriptions across studies, these histopathological findings serve as essential diagnostic criteria for BBC, facilitating its differentiation from other odontogenic cysts. This review aims to provide a comprehensive analysis of the multifaceted nature of BBC, setting the stage for a detailed exploration of its clinical, radiographic, and histologic characteristics, and its implications for patient management, which can ultimately help direct the clinical approach to this lesion.

2. Material and methods

This systematic review (registered at the International Prospective Register of Systematic Reviews (PROSPERO) CRD42023405169) was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). No financial support was received for this review.

2.1. POT question

Due to the aim of our systematic review to summarize knowledge about BBC, we addressed the following question: "What are the epidemiological characteristics of patients affected by BBC?". Using the Patient, Outcome, and Type of Study (POT) system, we organized the question to answer our purpose as follows.

P: patients with buccal bifurcation cyst;
O: epidemiological features;
T: observational studies.

2.2. Eligibility criteria

The included studies were observational (i.e., case reports, case series, case-control, cohort studies, and cross-sectional) and clinical trials involving patients with buccal bifurcation cysts restricted to the published English Language literature. The excluded studies included articles involving patients with other cysts, reviews, meta-analyses, letters, book chapters, conference works, and in vitro or animal studies.

2.3. Search strategy

The identification of studies for this systematic review was carried out through a careful search in five databases (Embase, LIVIVO, Pubmed, Scopus, and Web of Science), from September 8, 2023. The strategy was carried out meticulously using keywords selected according to the Medical Subject Headings [MeSH —National Center for Biotechnology Information (NCBI) and using terms following the WHO Classification of Tumors 2022 [4], being adapted for each database (Table 1). All articles were transferred to Mendeley and subsequently to Rayyan's online reference management tool.

2.4. Study selection

Two reviewers independently selected studies from the previous electronic search. The Kappa test was performed to assess agreement between examiners in the first screening stage, using the Minitab 19 software (Minitab Inc., State College, USA). The first stage of selecting was carried out using Rayyan, through the blinding mode, by reading titles and abstracts to exclude articles that did not meet the inclusion criteria. The potential studies selected were read in full to check eligibility in a second selection stage. Therefore, studies that met the selection criteria were selected for data extraction. At all stages of study

Table 1
The search strategy of the five databases.

Databases	Search strategy[a]
Pubmed	((((("Inflammatory collateral cysts") OR ("buccal bifurcation cyst")) OR ("mandibular infected buccal cyst")) OR ("mandibular buccal bifurcation cyst")) OR ("inflammatory paradental cyst")
Embase	'inflammatory collateral cysts' OR 'buccal bifurcation cyst'/exp OR 'buccal bifurcation cyst' OR 'mandibular infected buccal cyst'/exp OR 'mandibular infected buccal cyst' OR 'mandibular buccal bifurcation cyst' OR 'inflammatory paradental cyst'
Scopus	TITLE-ABS-KEY ("Inflammatory collateral cysts" OR "buccal bifurcation cyst" OR "mandibular infected buccal cyst" OR "mandibular buccal bifurcation cyst" OR "inflammatory paradental cyst")
Web of Science	((((ALL=("Inflammatory collateral cysts")) OR ALL=("buccal bifurcation cyst")) OR ALL=("mandibular infected buccal cyst")) OR ALL=("mandibular buccal bifurcation cyst")) OR ALL=("inflammatory paradental cyst")
LIVIVO	"Inflammatory collateral cysts" OR "buccal bifurcation cyst" OR "mandibular infected buccal cyst" OR "inflammatory paradental cyst"

[a] All search strategies were made on September 8, 2023. The terms followed the WHO Classification of Tumors 2022.

selection, disagreements were resolved by consensus between the examiners and, when necessary, a third reviewer was requested.

2.5. Data extraction

Data were extracted, by two examiners, based on the general and specific characteristics of the included studies, extracting clinical information (i.e. age, gender, lesion location; symptomatology; clinical presentation; vitality of associated tooth), histological, imaging findings (i.e. periapical and panoramic radiographic, computed tomography – to extract information such as injury aspects and size), diagnostic methods, follow-up, treatment modalities, recurrence and final diagnosis.

2.6. Risk of bias assessment

The risk of bias in the included studies was assessed by two reviewers independently. The methodological quality of case reports and case series were evaluated using the framework for appraisal suggested by Murad et al. [16] based on the domains of selection, ascertainment, causality and reporting. The judgment of case reports and case series was made based on the issues considered most critical. Six points were awarded for studies of the highest quality. A total score equal to or below 2 was determined as "low quality," a score of 3 or 4 was determined as "moderate quality," and a score of 5 or 6 was determined as "high quality." Case-control and cross-sectional studies were evaluated using the Newcastle–Ottawa Scale [17]. Eight points were given to studies of the highest quality. A total score of less than 3 was determined "low quality", a score of 4 or 5 was determined "moderate quality" and a score of more than 6 was determined "high quality".

3. Results

After inter-examiner calibration in the article selection process, the Kappa result was 0.95. From 510 studies, 72 were read in full and 39 were selected because they met the eligibility criteria established previously (Fig. 1). The reasons for excluding articles can be seen in Fig. 1. The main characteristics of the included studies are presented in Table 2. According to demographic data, the average age of patients was 7.5 years, with a higher prevalence of males compared to females (Fig. 2). Of the 87 cases described in the literature, 33 were found in the American continent, 30 in Europe, 13 in Asia, 10 in Oceania and one not informed (Fig. 3). Information about skin color is relevant to investigate possible lesion predilections; however, unfortunately, these data could not be obtained, as in most studies it was not reported. Of the 87 patients evaluated, eight were white-skinned (9.2 %) and one was black-skinned (1.1 %).

The maxilla (2 cases - 2.3 %) was the least affected anatomical area, with the BBC demonstrating a predilection for the jaw (85 cases - 97.7 %), which was more often affected unilaterally (58 cases - 66.6 %) than bilaterally (28 cases - 32.2 %). Notably, among unilateral cases, a slightly higher incidence was observed on the left side (32 cases - 56.1 %) compared to the right (25 cases - 43.9 %). Painful symptoms were reported in 27.6 % of patients (n = 24), while 20.7 % did not present any symptoms (n = 18) and 51.7 % did not provide information (n = 45)

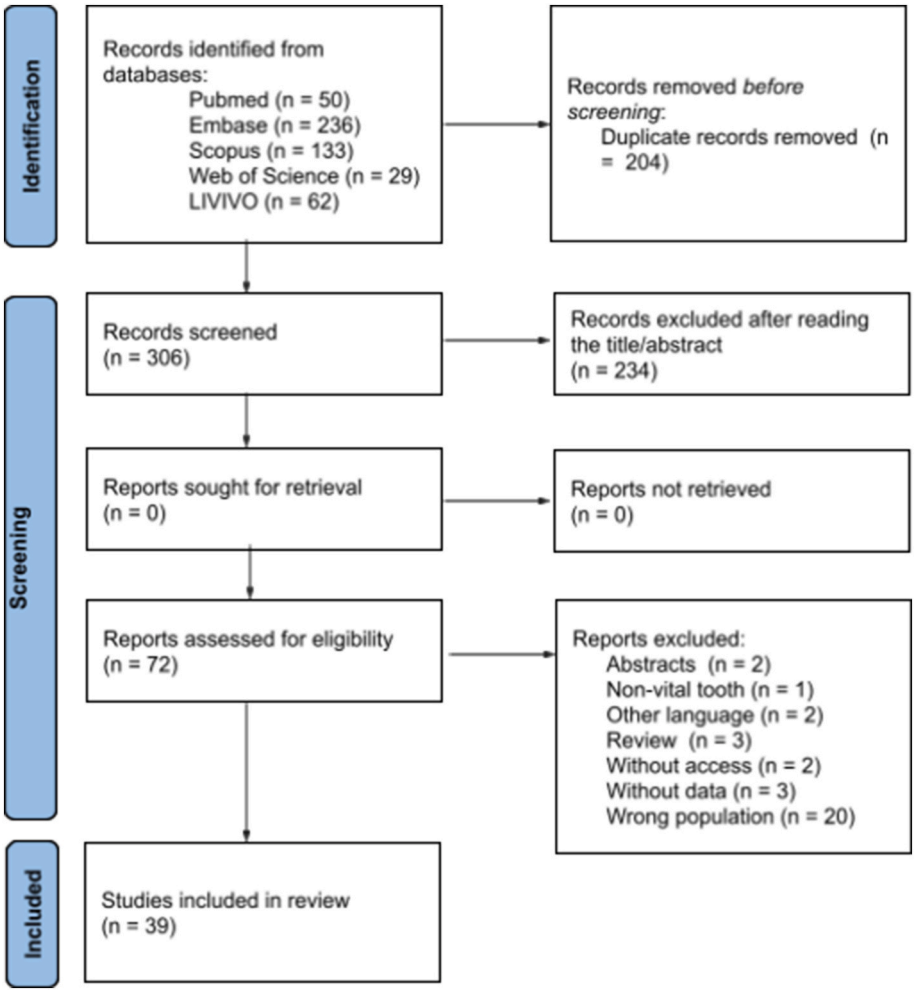

Fig. 1. Criteria for the selection of articles. Flow chart of methodology according to PRISMA guidelines.

Table 2
The main characteristics of the included studies.

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
Vedtofte and Holmstrup (1989) (15)	Denmark	18	NI	2nd upper molar	NI	NI	Nonkeratinized epithelium; inflamed capsule; foci of hemosiderin; cholesterol clefts	Enucleation, tooth extracted	NI	NI
		13	F	37,47	Periodontal pocket	Well-defined,bilateral unilocular ovoid radiolucency with sclerotic borders	Same as above	Enucleation	NI	NI
		7	M	46	Periodontal pocket	Radiolucency associated to affected tooth	Same as above	Enucleation	NI	NI
		7	M	36	NI	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex	Same as above	Enucleation	NI	NI
Wolf and Hietanen (1990) (35)	Finland	6	F	46	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Non-keratinized epithelium; heavy/mixed inflammation in capsule; neutrophilic exocytosis	Enucleation, tooth preserved	NI	No
		7	M	36	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Same as above	Enucleation, tooth preserved	2 years	No
		9	F	46	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Same as above	Enucleation, tooth preserved	1.5 year	No
		12	F	37	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Same as above	Enucleation, tooth extracted	6 years	No
		13	F	47	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Same as above	Enucleation, tooth preserved	2 years	No
		14	F	37	NI	Radiolucency demarcated by concave layer of dense bone with a diffuse border	Same as above	Enucleation, tooth extracted	1 year	No
El-Magboul et al. (1993) (30)	United Kingdom (England)	7	F	36	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and proliferative periostitis of the buccal cortex;	Arcaded spongiotic epithelial lining; dense inflammation in capsule	Enucleation, curettage, tooth preserved	NI	NI
Thurnwald et al. (1994) (18)	Australia	8	F	36,46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth; Expansion of the buccal cortex	Non-keratinized epithelial lining; mildly inflamed capsule, non-proliferating epithelial rests	Enucleation	NI	No
		8		36	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth; Expansion of the buccal cortex	Non-keratinized epithelial lining; hyaline bodies; chronic inflammation in capsule; giant cells; inactive epithelial rests			
		9		36	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth	Hyperplastic epithelial lining; chronically inflamed capsulel			
		5	M	36	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth	Same as above	Marsupialization		

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Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
		7		36,46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth; Expansion of the buccal cortex	Same as above	Enucleation		
		7		36,46	Intraoral (gingiva) bilateral swelling	Radiolucency associated to affected tooth	Same as above			
		7		46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth; Expansion of the buccal cortex; Cortical perforation	Non-keratinized epithelial lining; heavily inflamed capsule			
		7		46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth	Non-keratinized epithelial lining; heavily inflamed capsule			
		8		46	Intraoral (gingiva) unilateral swelling; Purulent Material		Non-keratinized epithelial lining; heavily inflamed capsule; giant cells			
		9		46	Intraoral (gingiva) unilateral swelling		Non-keratinized epithelial lining; mildly inflamed capsule			
Thompson et al. (1997) (22)	NI	11	F	36	Intraoral (ginigva) unilateral swelling; Periodontal pockets; Purulent material; Unerupted tooth	Well-defined unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of affected teeth	NI	NI	1 Year	No
David et al. (1998) (53)	Canada	7	M	36,46	Extraoral unilateral swelling; Bucal tilting of associated teeth; Periodontal pockets	Radiolucency demarcated by concave layer of dense bone with a diffuse border	No	Bilateral spontaneous resolution	NI	No
		8		36,46	Extraoral bilateral swelling; Bucal tilting of associated teeth; Periodontal pockets	NI			1.7 years	No
		9		36,46	Bucal tilting of associated teeth; Periodontal pockets	Radiolucency demarcated by concave layer of dense bone with a diffuse border	NI	Left side: spontaneous resolution; Right side: Surgical approach	9 months	NI

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Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
Lobos et al. (2000) (25)	Chile	9	NI	46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth	Stratified squamous epithelial lining with arciform hyperplasia	Enucleation, tooth extracted	NI	NI
Annibali et al. (2002) (50)	Italy	7	F	36,46	Intraoral (gingiva) unilateral swelling	Well-defined bilateral unilocular ovoid radiolucency with sclerotic borders; Resorption of deciduous tooth root; Displacement of permanent tooth	NI	Left side: Marsuapialization, extraction of 75 and 36, enucleation of residual cystic cavity; Right side: Enucleation and extraction of 46	6 years	No
Lim et al. (2002) (38)	Singapore	13	F	37,47	Intraoral (gingiva) unilateral swelling	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Displacement of permanent molar	Nonkeratinized stratified squamous epithelium; chronically inflamed capsule	Enucleation, tooth preserved	NI	NI
Shohat et al. (2003) (19)	Israel	8	F	46	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Nonkeratinized stratified squamous epithelium with variable thickness; chronically inflamed capsule	Enucleation, tooth extracted	2–3 years	No
		8		46	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders		Enucleation		
		11		47	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders		Enucleation, tooth extracted		
		8	M	36,46	Intraoral (gingiva) bilateral swelling	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders		Enucleation		
		13	M	37,47	Intraoral (gingiva) bilateral swelling					
Naclerio-Homem et al. (2004) (33)	Brazil	15	F	47	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth	Non-keratinizing epithelial lining; chronically inflamed capsule	Surgical removal, osteotomy	NI	NI
Robledo et al. (2004) (51)	United States	12	M	37	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Stratified squamous epithelial lining; acute and chronically inflamed capsule	Curettage	NI	NI
Gallego et al. (2007) (26)	Spain	8	M	36,46	Intraoral (gingiva) unilateral swelling	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex	Non-keratinized stratified squamous epithelium with areas of hyperplasia; chronically inflamed capsule	Left side: Enucleation, tooth preserved; Right side: Spontaneous resolution	1 year	NI
Iatrou et al. (2009) (39)	Greece	7	M	NI	NI	NI	NI	Enucleation	NI	NI
		8		46	NI			Enucleation, tooth extracted		
		8		46	NI					
		9		36	NI					
Borgonovo et al. (2010) (34)	Italy	7	M	36	Intraoral (gingiva) unilateral swelling; Unerupted tooth	Radiolucency demarcated by a fine radiopaque line	Hyperplastic nonkeratinized squamous epithelium; exocytosis; heavy acute and chronic inflammation in capsule; multinucleated giant cells	Enucleation	1 year	No

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Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
		8		36	Intraoral (gingiva) unilateral swelling; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Nonkeratinized, stratified squamous epithelial lining with areas of hyperplasia; chronically inflamed capsule			
Thikkurissy et al. (2010) (28)	United States	7	M	46	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling; Periodontal pockets; Tenderness; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and proliferative periostitis of the buccal cortex; Displacement of the permanent molars	Non-keratinized stratified squamous epithelial lining with focal hyperplasia; exocytosis; chronic inflammation and erythrocytes extravasated in capsule	Enucleation, tooth preserved	1, 2, and 14 months	No
Zadik et al. (2011) (54)	Israel	7.5	NI	36,46	Extraoral bilateral swelling; Tenderness	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders	No	Self resolved within 5 months	NI	No
Corona-Rodriguez et al. (2011) (20)	Mexico	7	M	36,46	Extraoral bilateral swelling; Intraoral (gingiva) unilateral swelling; Tenderness; Tooth partial eruption	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders	Nonkeratinized stratified squamous epithelial lining; chronic inflammation in capsule; cords and islands of odontogenic epithelium	Enucleation, teeth preserved	3 and 6 months	No
Damm (2011) (41)	United States	13	M	37,47	Extraoral bilateral swelling; Buccal tilting of associated teeth	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders	Proliferative stratified squamous epithelial lining; heavy exocytosis	Enucleation	NI	NI
Ferreira et al. (2011) (49)	United States	8	M	36	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected tooth; Cortical perforation; Lingually displacement of the roots	Proliferative stratified squamous epithelial lining; intense chronic inflammation in capsule	Enucleation, tooth extracted	NI	NI
Santos et al. (2011) (31)	Brazil	8	NI	36	Intraoral (gingiva) unilateral swelling; Periodontal pocket	Radiolucency associated to affected tooth; Cortical perforation;	Nonkeratinized stratified squamous epithelial lining with hyperplastic area; chronic inflammation in capsule	Enucleation	6 months	No
Boffano et al. (2012) (42)	Italy	9	NI	36,46	Extraoral bilateral swelling	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Cortical erosion and perforation	Non-keratinized stratified squamous epithelium; chronically inflamed capsule	Enucleation, teeth preserved	15, 30, 45 and 60 days; 6 months	No
Ramos et al. (2012) (52)	Brazil	9	M	36,46	Extraoral unilateral swelling; Intraoral	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex	Thin non-keratinized stratified squamous epithelium; chronically inflamed capsule	Surgical curettage, enucleation	Approximate 1 year	No

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Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
					(gingiva) bilateral swelling; Purulent material; Tooth partial eruption; Unerupted tooth					
Issler et al. (2013) (11)	France	8	F	36,46	Intraoral (gingiva) bilateral swelling; Tooth partial eruption; Unerupted tooth	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Non-keratinized stratified squamous epithelium; variable thicknesses; chronically inflamed capsule	Osteotomy, enucleation, teeth preserved	2, 10 and 18 months	No
		9	M	46	Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Cortical perforation; Buccal displacement of permanent affected tooth and displacement of the second premolar	NI	Cyst removal, tooth preserved	2–3 months	NI
Borgonovo et al. (2013) (40)	Italy	14	F	37	Normal appearance	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Arcading, proliferating non-keratinized stratified squamous epithelial lining; exocytosis; acute and chronically inflamed capsule	Ostectomy, enucleation, tooth preserved	6 months	Partially regression of the lesion
Borgonovo et al. (2014) (27)	Italy	6	M	46	Intraoral (gingiva) unilateral swelling; Periodontal pocket	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Arcading, proliferating non-keratinized stratified squamous epithelial lining; chronic and acutely inflamed capsule	Osteotomy, enucleation, tooth preserved	NI	NI
Levarek et al. (2014) (16)	United States	6	F	36	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots; Periosteal reaction resembling an "onion-skin" appearance	Non-keratinized stratified squamous epithelium; inflamed capsule	Surgical approach, debrided of the granulation-like tissue, Cancellous bone was placed in the defect and a resorbable membrane was placed over the graft site	9 months	No
		7		36	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling; Tenderness; Unerupted tooth	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Non-keratinized stratified squamous epithelial lining with hyperplastic areas; inflamed capsule	Incisional biopsy and complete excision, curettage, tooth preserved. The defect was grafted with cancellous bone and a resorbable membrane was placed	5 months	
		7	M	36	Extraoral unilateral swelling; Intraoral	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of	Non-keratinized stratified squamous epithelial lining with hyperplastic areas; inflamed capsule	Excisional biopsy	2 years	

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Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
					(gingiva) unilateral swelling; Periodontal pocket	permanent affected tooth with lingually displacement of the roots				
Friedrich et al. (2014) (32)	Germany	6	M	36	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Non-keratinized squamous stratified epithelial lining with variable thickness; chronic and acutely inflamed capsule; D2-40 immunostain showing strongly marked basal epithelial cells, negative in stroma	Surgical approach	15 months	Not clear
De Grauwe et al. (2018) (17)	Belgium	8	F	36	NI	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Cortical perforation; Proliferative periostitis of the buccal cortex	Vestibular cyst with acute and chronic inflammation	Osteotomy, enucleation and curettage	2 years	No, but a slight bone defect was present on the buccal area at the site of the bifurcation
		6	M	36	Tenderness; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Cortical perforation; Proliferative periostitis of the buccal cortex	Non-keratinized squamous epithelial lining; fibrinopurulent material and granulation tissue with mixed inflammatory infiltrate	Osteotomy, enucleation and curettage	NI	NI
	Greece	7		46	Normal appearance	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Cortical perforation; Proliferative periostitis of the buccal cortex	Non-keratinized squamous epithelial lining with elongated and interconnected rete pegs and exocytosis; inflamed cystic capsule	Enucleation, curettage, tooth extracted		
Kim et al. (2018) (43)	Korea	8	M	46	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling; Tenderness; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Hyperplastic non-keratinized stratified squamous epithelial lining; chronically inflamed capsule	Enucleation, tooth preserved	5 months; 2 years	No
		9		36	Extraoral unilateral swelling; Buccal tilting of associated teeth	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Buccal displacement of permanent affected tooth with lingually displacement of the roots			6 months	
Bautista et al. (2019) (23)	Brazil	7	F	36,46	Intraoral (gingiva) bilateral swelling	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Non-keratinized stratified epithelial lining; exocytosis and spongiosis; chronically inflamed capsule	NI	NI	NI
Derindag et al. (2019) (44)	Turkey	10	M	46	Extraoral unilateral swelling; Intraoral	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex;	NI	Enucleation, tooth preserved	NI	NI

(*continued on next page*)

Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
					(gingiva) unilateral swelling	Buccal displacement of permanent affected tooth with lingually displacement of the roots; Periosteal reaction resembling an "onion-skin" appearance				
Lima et al. (2019) (29)	Brazil	7	M	46	Extraoral unilateral swelling; Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Non-keratinized squamous epithelial lining with arcading pattern; spongiosis and exocytosis; chronically inflamed capsule; few giant multinuclear cells	Enucleation	7 months	No
Aloyouny et al. (2020) (21)	Saudi Arabia	7	M	36,46	Extraoral bilateral swelling; Intraoral (gingiva) biilateral swelling; Unerupted tooth	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders	Non-keratinized stratified squamous epithelial lining; mixed inflammatory reaction and surrounding edematous granulation tissue; degenerated bony spicules	Enucleation, curettage, teeth preserved	6 and 12 months	No
Dave et al. (2020) (45)	United Kingdom	6	F	36,46	Intraoral (gingiva) unilateral swelling	Radiolucency associated to affected teeth; Expansion of the buccal cortex	Generic information; confirmed inflammatory odontogenic cyst	Enucleation, teeth preserved	6 months	No
		11	M	36,46	No alteration	Well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders	Generic information; confirmed inflammatory odontogenic cyst	Enucleation with preservation of 36		
Dos Santos et al. (2021) (46)	Brazil	6	F	46	Intraoral (gingiva) unilateral swelling; Periodontal pocket; Tooth partial eruption	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Cortical perforation	NI	Enucleation, tooth preserved	45 days, 3 and 12 months	No
Liu et al. (2022) (47)	China	6	F	36	Extraoral unilateral swelling; Tooth partial eruption	Radiolucency associated to affected tooth	Non-keratinized stratified squamous epithelial lining; mixed inflammatory infiltrate	Enucleation, curettage	One and a half years	No
		8	M	36	Extraoral unilateral swelling; Purulent material	Radiolucency associated to affected tooth	Thin non-keratinized stratified squamous epithelial lining; chronic inflammation	Curettage		
Ruddocks et al. (2022) (48)	United States	8 8 9 12 8 8 8 9 9	F M 	36 46 46 37,47 46 36 36,46 36,46 36	NI NI NI NI NI NI NI NI NI	Radiographs were available for 9 of 10 cases. All cases were well defined, with (60 %) or without (30 %) a corticated border. Displacement of roots of the associated teeth or a substantial difference in height between buccal and lingual cusps was observed in 7 of 10 cases (70 %).	NI	NI Enucleation NI Enucleation NI	NI 5 months NI 	NI

(*continued on next page*)

Table 2 (*continued*)

Author (Year)	Country	Age (years)	Gender	Tooth involved	Clinical findings	Radiological findings	Histological findings	Treatment	Follow-up	Recurrence
		11		47	NI	Three cases (30 %) exhibited perforation of the buccal cortical plate				
Jajam et al. (2023) (12)	Chile	6	F	46	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex	Non-keratinizing stratified epithelial lining with variable thicknesses; inflamed capsule	Enucleation, teeth preserved	After 2 years	No
		8		36,46	Intraoral (gingiva) bilateral swelling	Radiolucency associated to affected teeth; Buccal displacement of permanent affected tooth with lingually displacement of the roots	Thin non-keratinized stratified squamous epithelial lining with focal hyperplastic areas; exocytosis; chronically inflamed capsule with extravasated erythrocytes		8 months	
		8		36,46	Intraoral (gingiva) unilateral swelling; Purulent material	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex	Non-keratinizing stratified epithelial lining with abscess formation		9 months/after 2 years	
		9		26	Intraoral (gingiva) unilateral swelling	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders	Non-keratinizing stratified epithelial lining with variable thickness, arciform growth; mixed inflammation in capsule		1–2 years	
		8	M	36	Intraoral (gingiva) unilateral swelling; Purulent material	Well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders; Expansion and perforation of the buccal cortex	Non-keratinizing stratified epithelial lining; acutely inflamed capsule		2 years	

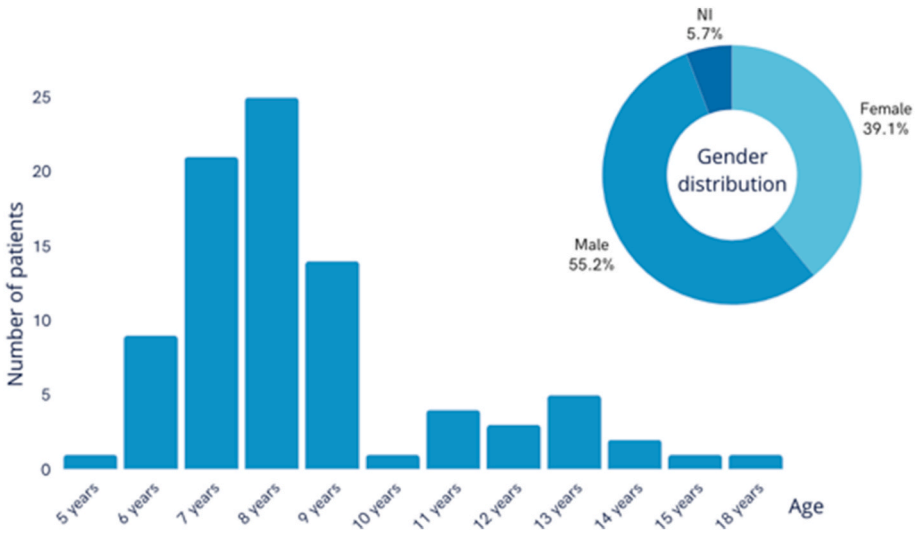

Fig. 2. Demographic data of included patients.

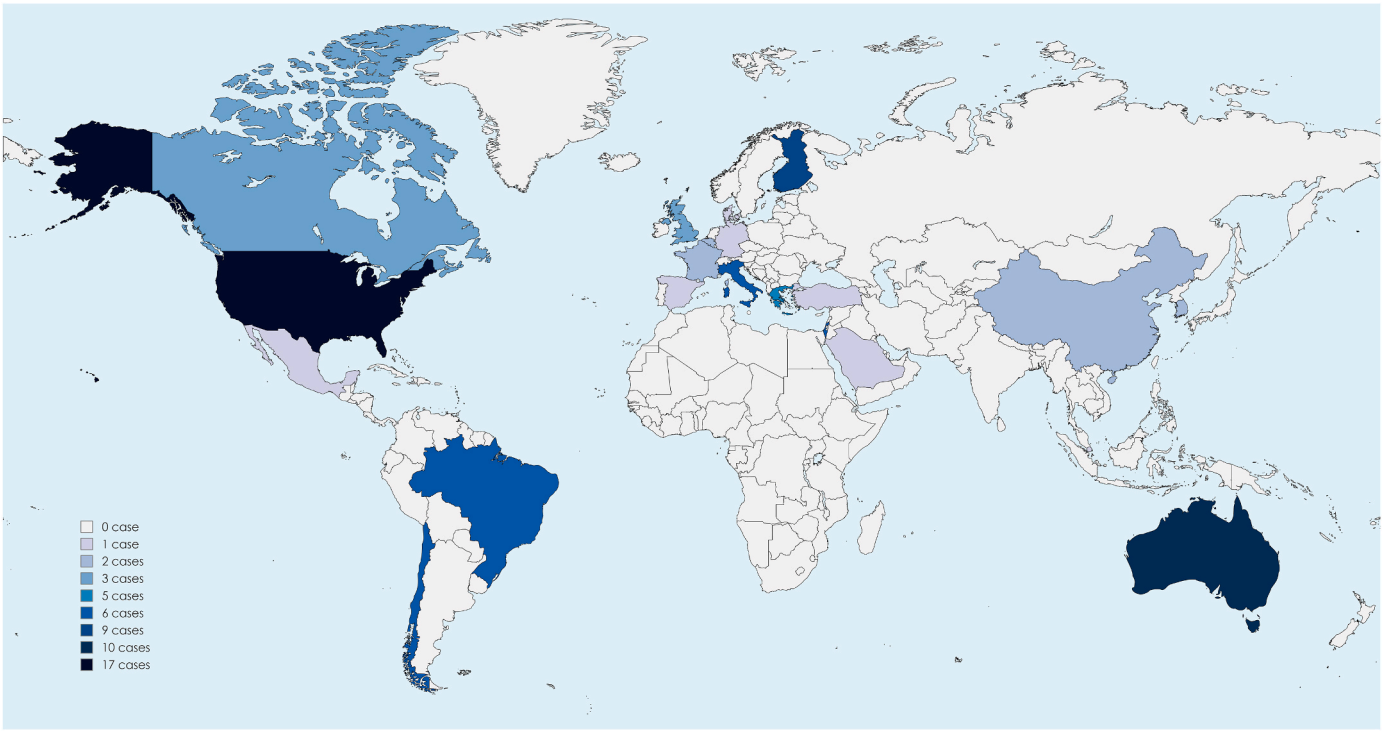

Fig. 3. Geographical location of the included studies.

about their condition. Concerning the affected teeth, the first permanent molars (93 teeth - 82.3 %) were the most affected, followed by the second permanent molars (18 teeth - 15.9 %). There was only one case of lower primary second molar (One tooth - 0.9 %) involvement, and one case (0.9 %) was not reported.

The most related alteration was gingival unilateral swelling (40 cases - 46 %), followed by extraoral unilateral swelling (14 cases - 16 %) and involved tooth partially erupted (11 cases - 12.6 %). An interesting finding was buccal periodontal pockets in the affected teeth, which varied between 4.5 and 15 mm, being related in 11 cases (12.6 %). Gingival bilateral swelling (8 cases - 9.2 %), extraoral bilateral swelling (6 cases - 6.9 %), tenderness (6 cases - 6.8 %), purulent discharge material (6 cases - 6.8 %), unerupted tooth (6 cases - 6.8 %), and buccal tilting of the associated tooth (5 cases - 5.7 %) were the least clinical changes. Erythematous and inflamed soft tissues were reported only in 2 cases (2.2 %). Unfortunately, 26.4 % of the included cases did not report any clinical manifestation.

Radiological features showed the prevalence of well-defined, unilateral unilocular ovoid radiolucency with sclerotic borders in 27 cases (31 %); expansion of the buccal cortex in 22 cases (25.3 %); radiolucency associated with the affected tooth in 19 cases (21.8 %); radiolucency measure in 19 cases (21.8 %), which varied between 8 and 30 mm considering its greatest extent; cortical perforation or resorption in 16 cases (18.4 %); 15 cases (17.2 %) were described as well-defined, bilateral unilocular ovoid radiolucency with sclerotic borders; displacement of the permanent affected tooth with the root apices toward the lingual cortical plate in 14 cases (16.1 %); 9 cases (10.3 %) revealed radiolucency demarcated by dense bone with a diffuse border

in all limits or a fine line. Proliferative periostitis of the buccal cortex was present in 7 cases (8 %), being a periosteal reaction resembling an "onion-skin" appearance in 2 cases; and permanent molar (not the affected tooth) or premolar bud displacement was seen in 4 cases (4.5 %). 17 cases (19.5 %) did not report any radiographic or tomographic description of each lesion.

Histologically, the lesions were characterized by the recurrent presence of a cystic capsule lined by a non-keratinized and hyperplastic stratified squamous epithelium, with the occasional presence of spongiosis, and exocytosis in some areas. Furthermore, the fibrous cystic capsule was marked by a chronic inflammatory infiltrate comprised of lymphocytes, and plasma cells, however occasionally showing the presence of neutrophils and eosinophils. Histopathological Information from 23 cases (23.4 %) was not included in this analysis due to the lack of available histological assessments. It was important to note that in the majority of the studies (61 cases - 70.1 %), the diagnosis of BBC was established after clinical, radiological, and histopathological examination.

The predominant treatment for BBC involved a variety of approaches, with enucleation alone being the most common (48 cases - 55.2 %), followed by combination enucleation and curettage (5 cases - 5.7 %), cystectomy (4 cases - 4.6 %), osteotomy and curettage (3 cases - 3.4 %) and isolated marsupialization (1 case - 1.1 %). Other approaches involved the association of procedures and/or spontaneous resolution. In 10 cases (11.5 %) the treatment carried out was not informed. In 52 cases (59.8 %) the involved tooth was preserved while in 12 cases (13.8 %) it was extracted. In 23 cases (26.4 %) information was not available on whether or not the affected tooth had been extracted. The follow-up period ranged from 15 days to 6 years. The majority of patients did not experience recurrence of the lesion (54 cases - 62.1 %) during the follow-up period. Only one case had partial regression of the cyst (1.1 %), while 32 cases (36.8 %) were not reported.

Interestingly, the nomenclature used for the final diagnosis in the cases of the included studies showed a wide variation (Fig. 4), but the similarity in the clinical, radiographic, and histological findings of the registered cases is notable. Therefore, there seems to be an error in using the correct nomenclature in some cases.

3.1. Quality assessment

In the methodological quality assessment of case series and case reports, 35 (94.6 %) studies were considered to be high quality, 2 (5.4 %) with moderate quality, and none with low quality (Suppl Table 3). The quality assessment of cohort studies can be seen in Suppl Table 4, being all studies classified as high quality.

4. Discussion

BBC was classified as a rare inflammatory odontogenic cyst in the 1992 World Health Organization (WHO) classification of odontogenic tumors and cysts [4]. There is a challenge in diagnosing this lesion, as its histopathology is non-specific, being like other inflammatory cysts, such as paradental and radicular cysts [18,19]. Therefore, the correlation between clinical, radiological, and histopathological findings is important for an accurate diagnosis and adequate treatment of the lesion [19]. Due to the similarity of BBC with other odontogenic cysts, this work aimed to synthesize clinical, radiological, and histopathological data to help clinicians in the diagnosis and proper therapeutic approach of this pathology.

The classification history of the buccal bifurcation cyst has evolved as the understanding of its etiology and histopathological features has expanded. The initially coined term for this pathosis was mandibular infected buccal cyst-molar area in 1983 [1], and several other names have been employed ever since, including circumferential dentigerous cyst [2,20], buccal bifurcation cyst (BBC) [3] and juvenile paradental cyst [20]. The term BBC describes the lesion's specific anatomical location and its association with mandibular first and second molars [21].

The WHO 1992 classification emphasized the inflammatory nature of the lesion and its distinct histopathological features compared to other odontogenic cysts. BBC classification as an inflammatory odontogenic cyst remains unchanged in the most current WHO classification, under inflammatory collateral cysts (ICC) and alongside paradental cyst [4], highlighting its unique position within the spectrum of odontogenic lesions. Up-to-date, WHO still brings the term "mandibular infected buccal cyst" as an acceptable designation for BBC [4].

Furthermore, BBC etiology is attributed to inflammation in the pericoronal tissues, which may be exacerbated by factors such as food impaction or the presence of enamel projections on the buccal aspect of the tooth [12,14]. Pathogenically, ICCs are characterized as "pocket" cysts resulting from dilation of the pericoronal tissues; ICCs are lined by sulcular or junctional epithelium derived from the reduced enamel epithelium [12,13]. Therefore, *in contrast to* (differently from) radicular cysts, the eligible criteria for BBC includes the association with a

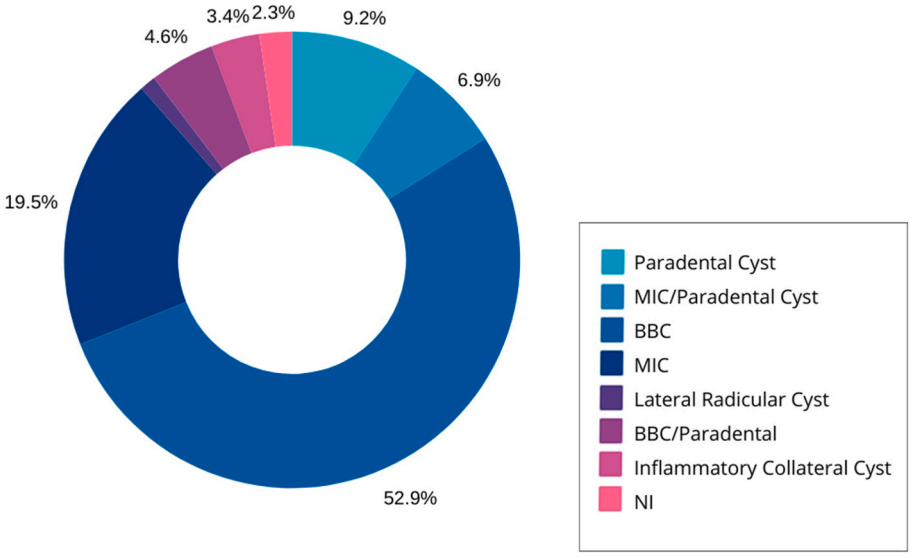

Fig. 4. Nomenclature used for the final diagnosis in the cases of the included studies. MIC (mandibular infected cyst); BBC (buccal bifurcation cyst); NI (not informed).

partially or recently erupted tooth that is vital; and differently from dentigerous cysts, a radiolucency distinct from a dental follicle [4].

Epidemiologically, ICCs account for approximately 5 % of odontogenic cysts and are more prevalent in males (around 70 % of cases). The average age of presentation is around 9 years old for lesions associated with the first molar and 17 years old for those linked with the second molar [12,15]. As extracted from our review, and according to the relevant literature, the mean age of BBC was 7.5 years old. Interestingly, odontogenic cysts are the most frequent jaw lesions in pediatric patients, being the majority of lesions localized on the posterior mandible [22], which highlights the importance of knowing the diagnostic aspects of BBC and considering this entity in the differential diagnosis of mandibular cysts.

By definition, BBC should be located on the buccal or distobuccal aspect of partially erupted or recently erupted teeth [15,23]. BBCs predominantly occur adjacent to the buccal aspect of mandibular first or second molars; bilateral occurrence has been reported in about 25–35 % of cases [4]. Rarely and rather unexplainably, ICC (4 %) has been reported in other sites, and that happened with two cases included in this review [19,23], which were located on the maxilla. Clinical manifestations of BBC often include signs of infection such as pain, tenderness, and suppuration [4].

The most common clinical manifestations included unilateral gingival swelling and extraoral swelling. This evidence is noted due to cortical bone buccal expansion that varies according to the size of the cyst [19,24–26]. Cyst dimensions were frequently found to vary between 1 and 3.0 cm [24,27–29]. The presence of the cyst can cause the affected tooth to tilt towards the buccal side, accompanied by deep periodontal pockets [15,30]. We found, in 11 cases, patients with periodontal pockets varying between 9 and 15 mm. BBCs can be confused with aggressive localized periodontitis and lead to erroneous treatment decisions. So, imaging evaluation is essential to guide the correct diagnosis [31].

Radiographically, BBCs have been observed to extend towards the lower border of the mandible and frequently exhibit periosteal reaction with the formation of laminated new bone [15]. A well-defined, unilateral unilocular ovoid radiolucency lesion with sclerotic borders or just radiolucency associated with the affected tooth both involved the furcation area were predominant in the present review, but that can be found in other odontogenic cysts such as dentigerous cyst, odontogenic keratocyst or radicular cyst [22], which indicates that BBC does not possess specific radiographic criteria, possibly representing a challenge to clinicians, including pediatric dentists and oral pathologists. Imaging studies reveal corticated radiolucencies situated over the buccal or distobuccal region of the affected tooth, with an intact lamina dura and a normal follicular space surrounding the partially erupted tooth [14].

Regarding the histopathological findings of BBC, several consistent characteristics were noted, and some particularities are worth mentioning. Regarding the cystic epithelial lining, BBC was consistently lined by non-keratinized stratified squamous epithelium; as expected, lack of keratinization is a key finding of BBC, as only a few odontogenic cysts exhibit keratinization, i.e., odontogenic keratocyst (OKC) or *ortho*-keratinized odontogenic cyst (OOC) [32]. The cystic epithelium of BBC exhibited hyperplasia and arciform growth in various studies [5,19,33–35], which is rather nonspecific. Some studies also mentioned the presence of spongiosis in the epithelial lining [31,36,37]. In fact, spongiosis is not a specific finding and may be encountered in inflammatory odontogenic cysts, e.g., radicular cysts, or secondarily inflamed developmental odontogenic cysts, e.g., inflamed dentigerous cysts.

There was consistent presence of an inflammatory infiltrate within both the epithelial lining (exocytosis) and the connective tissue wall of the cysts. More specifically, this infiltrate included various types of inflammatory cells such as neutrophils, lymphocytes, plasma cells, and eosinophils. Some references specifically mentioned the presence of intense chronic inflammatory infiltrate within the cystic capsule [34,38–40]. Additionally, multinucleated giant cells were observed in some cases [36,41]. Again, the inflammatory infiltrate of odontogenic cysts is somewhat not specific and can be more or less pronounced depending on the etiology of the cystic lesion or the presence of a concomitant infection. In addition, any odontogenic cyst may be prone to rupture phenomenon, which often leads to cholesterol cleft formation and adjacent infiltration by multinucleated giant cells.

As expected, the connective tissue wall of the cysts was composed of fibrous connective tissue, and apart from signs of inflammation, the cystic wall may have shown vascular proliferation, or edematous granulation tissue [5,25,27,29]. Less commonly, the presence of hemosiderin pigment deposition and cholesterol clefts were identified in the connective tissue wall [42]. Contrastingly though, the WHO classification of tumors brings cholesterol deposition and the presence of foamy histiocytes as being frequently observed in BBC [4]. Other histopathological features included abscess formation [19], and the presence of odontogenic epithelium islands [28]. The presence of odontogenic epithelial islands is nonspecific and has been associated with some odontogenic cysts, such as dentigerous cysts and radicular cysts, and depending on their respective morphology these odontogenic islands have been termed squamous odontogenic tumor (SOT)-like proliferation [43,44].

Overall, while there are variations in the descriptions provided across different references, the histopathological findings consistently characterize buccal bifurcation cysts as lined by non-keratinized stratified squamous epithelium with varying degrees of hyperplasia and potentially associated with a chronic inflammatory infiltrate within the connective tissue wall. The histological features of BBC closely resemble those of a radicular cyst, with both typically exhibiting an inflamed wall lined by hyperplastic non-keratinized epithelium. Additionally, the buccal bifurcation cyst may present an open connection with either pericoronal or gingival tissues [4]. Accordingly, essential diagnostic criteria for BBCs include the observation of non-keratinized epithelium [4].

In terms of treatment, enucleation of BBC is the standard approach [4], and molars affected by BBCs can typically be conserved, with normal eruption patterns expected post-treatment [4]. In fact, our review found that enucleation or cystectomy with tooth preservation was by far the most selected treatment for BBC (66.67 %) [6,7,18,19,27–29,33–38,42,45–53]. Nevertheless, other treatments approaches were also found in the literature, and those included cystectomy with tooth extraction (8.33 %) [5,23,54], enucleation with tooth extraction (5.56 %) [27,45], marsupialization and tooth extraction (2.78 %) [55], curettage (5.56 %) [21,56], excisional biopsy or excision (2.78 %) [24]. Also, 8.33 % of cases were associated with spontaneous resolution [33,57,58]; in fact, cases that resolved without surgery may have benefitted from daily irrigation of the buccal pocket with saline and hydrogen peroxide.

This systematic review also sheds light on the prognosis of BBC. Although many studies included in this review did not mention the presence or absence of recurrence (56.3 %), most studies that assessed recurrence potential stated no recurrences for BBC. Only one patient (1.15 % of all patients analyzed) experienced recurrence at a 5-month follow-up [24].

5. Conclusions

In summary, the intricate management differences between the BBC and its mimickers, including radicular cysts and dentigerous cysts, underscore the critical need for up-to-date insights into BBC's clinical, radiographic, and histologic characteristics. By consolidating the latest knowledge, this study aims to guide clinicians toward accurate diagnosis and tailored treatment strategies, thereby enhancing patient care and outcomes in the realm of maxillofacial pathology.

Matheus de Castro Costa: Formal analysis and interpretation of data, Rani Kanthan: acquisition of data, Marina Lara de Carli: Formal analysis and interpretation of data, Felipe Fornias Sperandio: conception and design, Formal analysis and interpretation of data

Ethics committee/institute for this study

Not applicable; systematic review of the literature.

Ethical approval

Not applicable; systematic review of the literature only.

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Declaration of competing interest

All authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.job.2025.100652.

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