Benign fibro-osseous lesions: A retrospective study of sixty-four cases from a single institute, Riyadh, Saudi Arabia

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ABSTRACT

Objective: Benign fibroosseous lesions (BFOLs) encompass a heterogenous collection of bone conditions characterized by replacing normal bone with fibro-collagenous tissue with osteoid or woven bone, and cementicles. Despite their clinical significance, the frequency of BFOLs in Saudi Arabia still needs to be assessed.
Methods: This retrospective study investigated the frequency and demographics of BFOLs in Riyadh, Saudi Arabia, by retrieving all cases recorded between January 1984 and January 2013 from a single Oral Pathology Laboratory archive.
Results: A total of 64 cases were classified as BFOLs, with a predominance in females (67.2 %) and a median age of 21.5 years. The most prevalent condition identified was fibrous dysplasia (45.31 %), followed by cemento-ossifying fibroma (26.56 %). There were significant sex differences between BFOLs, with a p-value of 0.03. FD was predominantly located in the maxilla (65.5 %), whereas COF was predominantly found in the mandible (82.3 %). Recurrence was observed in 17.2 % of patients with FD, in contrast to no reported recurrence in patients with COF.
Conclusion: This study represents the first exploration of BFOL frequency and demographics in Riyadh, Saudi Arabia, highlighting the need for further investigations to comprehensively understand the nature of these lesions in our population.

1. Introduction

Benign fibroosseous lesions (BFOLs) are an array of bony lesions with shared histopathological features. These conditions are characterized by fibro-collagenous tissue replacing the normal bone, often accompanied by deposition of osteoid, trabecular or woven bone, or cementicles (Mainville et al., 2017). The current World Health Organization (WHO) classification of BFOLs into developmental conditions, reactive/inflammatory, and neoplasms (Table 1) (Bishop et al., 2022). An accurate diagnosis of BFOLs typically requires a comprehensive assessment (Mainville et al., 2017). In other words, histological analysis of biopsied samples from BFOLs reveals overlapping characteristics. Although most cases can be identified by pathologists, definitive diagnosis often hinges on factors such as age, sex of the patient, and comprehensive clinical and radiographic evaluation. For example, fibrous dysplasia (FD), commonly seen in young adolescents, often manifests as diffuse radiopacity in the posterior maxilla with a distinctive "ground-glass"

appearance (Pereira et al., 2019).

Cemento-ossifying fibroma (COF), previously considered a neoplastic BFOL, is now classified as a mesenchymal odontogenic tumor (Nagao et al., 2017; Woo, 2015). Typically occurring in middle-aged females. COF affects the posterior mandible and exhibits various radiographic presentations depending on tumor maturation, ranging from entirely radiolucent to mixed radiopaque. However, it is always well-demarcated from the normal bone (Su et al., 1997; Woo, 2015). Conversely, cemento-osseous dysplasia (COD) is a reactive condition classically observed in middle-aged black females. The radiographic presentation of COD varies and can be classified as focal, apical, or florid. Other BFOLs include aggressive ossifying fibroma (AOF), commonly found in the sinonasal region, and rare familial gigantiform cementoma (FGC) (Su et al., 1997; Woo, 2015).

Reports on the frequency of BFOLs vary across different geographic regions, ranging from 32 to 276 cases, with a focus on clinicopathological features (Ogunsalu et al., 2001; Soluk-Tekkesin et al., 2022). The

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most recent data from Turkey identified COD as the most prevalent type of BFOLs (Soluk-Tekkesin et al., 2022), a trend that aligns with observations from South America (de Noronha Santos Netto et al., 2013). In contrast, FD appears to be more commonly encountered in China (Alsharif et al., 2009). Despite the detailed documentation of BFOLs' frequency and demographics globally, their status in Saudi Arabia remains unclear. Hence, our study aimed to present the first comprehensive analysis of BFOLs in Riyadh, Saudi Arabia, and to elucidate the demographic and clinical features of BFOLs in this specific geographic context.

2. Material and methods

This study entailed a retrospective examination of BFOLs, spanning 29 years (January 1984-January 2013), drawn from the Oral Pathology Laboratory archives at King Saud University in Riyadh, Saudi Arabia. The study procedures followed the Declaration of Helsinki and were approved by the College of Dentistry Research Center (IRB#FR0209). Data collected were stored in a secured electronic database with anonymized patient identities, accessible solely to authors. Due to the retrospective nature of this study, patient informed consent was waived.

Archival records from the oral pathology were scrutinized to manually identify BFOLs tagged as FD, COF, COD, cementoma, AOF, and FGC. Demographic and clinical data, including age, sex, and clinical and radiographic presentations, were retrieved from the final pathology reports. Additionally, hematoxylin and eosin-stained slides from all cases were reviewed by a certified oral pathologist (MA) and validated the histopathologic diagnosis. Our study used the diagnostic criteria outlined in the 5th edition of the WHO classification (Bishop et al., 2022).

The inclusion criteria for this study encompass patients demonstrating histopathological features consistent with BFOL diagnoses, including FD, COF, COD, AOF, and GFC. Only patients with comprehensive demographic, clinical, and radiographic data are considered eligible for inclusion. Conversely, exclusion criteria involve patients with incomplete clinical records or missing histopathological slides.

These criteria were established to ensure the inclusion of all BFOL cases in our archive and to minimize potential biases arising from incomplete data, aligned with the recent frequency report on BFOLs (Soluk-Tekkesin et al., 2022).

Descriptive analysis was performed using STATA 14.2 software (StataCorp.), including patient age, sex, location, recurrence, and complication. The correlations between different BFOLs and other variables were assessed using the chi-squared test for categorical variables (sex) and ANOVA for continuous variables (age). Statistical significance was set at a P value < 0.05 was considered statistically significant. Graphs were generated using the GraphPad Prism 9 software.

3. Results

There were 91 cases retrieved from the Oral Pathology Laboratory archive; 27 cases were excluded because of incomplete histories, missing radiographs, or histopathological slides. The final analysis included 64 cases of BFOLs, of which 43 (67.2 %) were observed in females, with a female-to-male ratio of 2:1 (Fig. 1A). The median age of BFOL patients was 21.5 years (range: 6—66 years), with four cases failing to document the patients' age. Most cases (75.0 %) were observed in the 2nd to 4th

decades of life (Fig. 1B). All patients were reported to be healthy except for two; one with asthma and one with hyperparathyroidism. The frequency of BFOLs is summarized in Fig. 1C.

3.1. Fibrous dysplasia

Fifteen females and 14 males aged 6–33 years, with a median age of 18, were included. Data were missing for two patients (Tables 2 and 3). Nineteen patients exhibited FD present in the maxilla, of which five extended to other craniofacial bones, such as the orbital bone, zygoma, and maxillary sinuses. The tomographic distribution of FD is illustrated in Fig. 2 A. The predominant clinical manifestation was a slowly growing, asymptomatic swelling, lasting between 3–108 months. Radiography showed poorly demarcated radiopacity with buccal and lingual cortical expansion. Ground glass appearance was also noted in two cases. Five patients had a history of disease recurrence after treatment.

3.2. Cemento-ossifying fibroma

Thirteen patients were female, with a ratio of 3.25:1. Their ages ranged from 12 to 55 years, with a median age of 32 (Tables 2 and 3). All patients, except one from the Philippines, were of Saudi nationality. The most frequent site was the mandible (82.3 %) (Fig. 2B). The typical clinical presentation was a painless, slowly growing expansion present for at least 1 month. Radiographically, COF appears as a well-demarcated unilocular lesion with a variable degree of radiopacity, with pushing borders or buccal expansion. No patient reported recurrence after treatment.

3.3. Cemento-osseous dysplasia

Patients with COD were exclusively females, with ages ranging from 35 to 66 and a median age of 41 (Tables 2 and 3). The tomographic distribution of COD is illustrated in Fig. 2C. Radiographically, COD exhibited irregular to well-defined radiopaque mass surrounded by a radiolucent rim. Two patients experienced pain and developed osteomyelitis. None of the cases showed recurrence after removal. Table 4 summarizes the demographics and distribution of different types of COD.

3.4. Aggressive ossifying fibroma

There were seven patients with AOF. Four patients were females, and three occurred in males aged 7–32 and a median age of 13 (Tables 2 and 3). Three tumors were located in the mandible (Fig. 2D). The patient presents with asymptomatic, bony swelling with well-delineated multilocular radiolucency and variable radiopacities measuring up to 5 cm. One patient reported teeth displacement. Histologically, four were psammomatoid, and two were trabecular variants. One patient showed recurrence.

Within this cohort, a single case of FGC was identified in a 21-year-old female. She exhibited maxillary and mandibular enlargement along with multiple impacted teeth.

Table 1
Fibro-osseous tumors and dysplasia, WHO 5th edition (Bishop et al., 2022)*.

Cemento-osseous dysplasia
Segmental odontogenic dysplasia
Fibrous dysplasia
Juvenile trabecular ossifying fibroma
Psammomatoid ossifying fibroma
Familial gigantiform cementoma

* Cemento-ossifying fibroma is reclassified as mesenchymal odontogenic tumor.
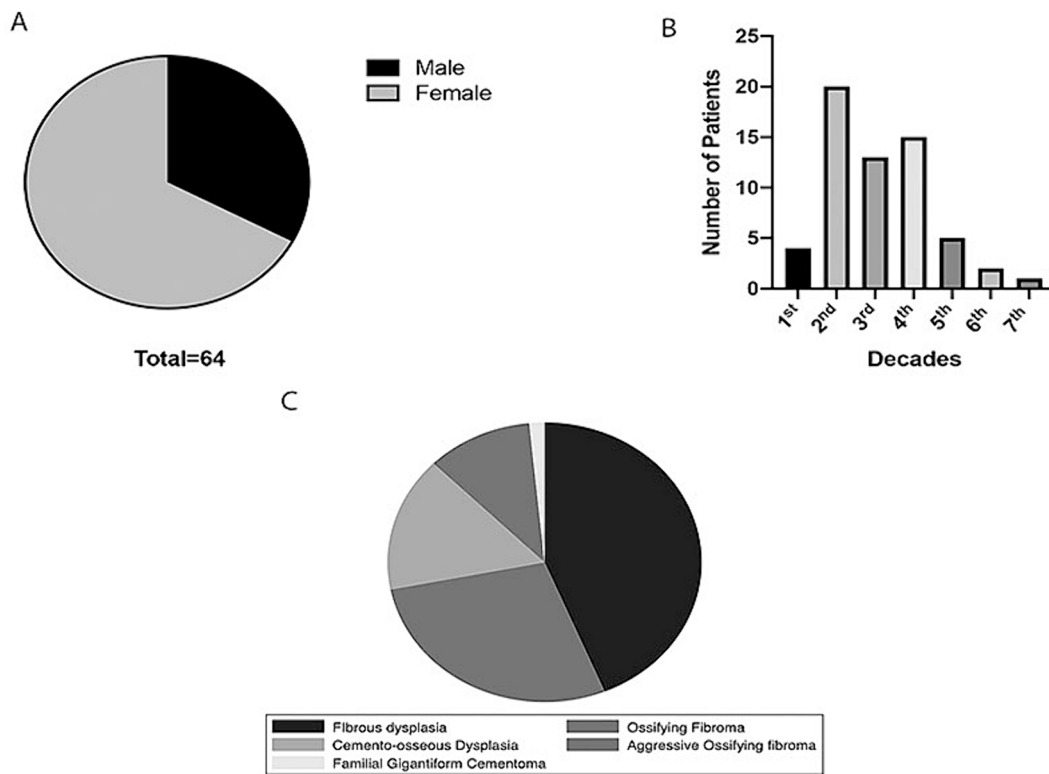
Fig. 1. Summary of the demographic and tumor frequency of all BFOLs. (A) Sex distribution of BFOLs, (B) Age distribution for BFOLs, (C) Different tumor and dysplasia frequencies of BFOLs.

Table 2
Sex distribution of BFOLs.

Type of lesions	Male		Female		Female: male ratio	p-value
	No.	%	No.	%		
Fibrous dysplasia	14	48.3 %	15	51.7 %	1.1:1	
Cemento-ossifying fibroma	4	23.5 %	13	76.5 %	3.25:1	
Cemento-osseous dysplasia	0	0	10	100 %	N/A	
Aggressive ossifying fibroma	3	42.9 %	4	57.1 %	1.3:1	
Familial gigantiform cementoma	0	0	1	100 %	N/A	
Total	21	32.8 %	43	67.2 %	2:1	0.03

4. Discussion

Understanding the population-based disease frequency within a specific geographic region is essential for enhancing disease awareness, precise diagnosis, and effective management. This knowledge provides healthcare professionals with a comprehensive overview of the disease spectrum in their region, empowering them to remain vigilant regarding early signs and symptoms. This heightened awareness leads to timely and accurate diagnoses, ensuring that patients receive the appropriate management. Although the frequency of BFOLs has been investigated worldwide, such as China, Thailand, and Brazil (Alsharif et al., 2009; de Noronha Santos Netto et al., 2013; Phattarataratip et al., 2014; Worawongvasu & Songkampol, 2010), there is a notable absence of studies on the frequency of BFOLs in Riyadh, Saudi Arabia. Therefore, this study aimed to assess the frequency of BFOLs within a Saudi population. Our findings revealed 64 patients with BFOLs, accounting for 1.28 % of all patients diagnosed within 29 years. This frequency aligns closely with the 1.0 % rate reported in Thailand (Phattarataratip et al., 2014). Other studies that reviewed BFOLs did not report the frequency of such lesions. However, Soluk-Tekkesin M et al. (Soluk-Tekkesin et al., 2022) documented 276 cases in Turkey, Muwazi LM, and Kamulegeya A (Muwazi & Kamulegeya, 2015) reported 155 cases in Uganda, Santos Netto et al.(de Noronha Santos Netto et al., 2013) reported 143 cases in Brazil, Worawongvasu W, and Songkampol K (Worawongvasu & Songkampol, 2010) reported 122 cases in Thailand, Alsharif MJ et al. (Alsharif et al., 2009) reported 127 cases in China, and Ogunslua CO et al. (Ogunsalu et al., 2001) reported 32 cases in Jamaica. These numbers are based on

Table 3
Age distribution of BFOLs.

Type of lesions	Age (years)								
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	Total	P-value
Fibrous dysplasia	1	15	8	3	0	0	0	27	0.0001
Cemento-ossifying fibroma	1	1	4	7	2	1	0	16	0.0001
Cemento-osseous dysplasia	0	0	0	4	3	1	1	9	0.001
Aggressive ossifying fibroma	2	4	0	1	0	0	0	7	0.0001
Familial gigantiform cementoma	0	0	1	0	0	0	0	1	N/A
Total	4	20	13	15	5	2	1	60*	

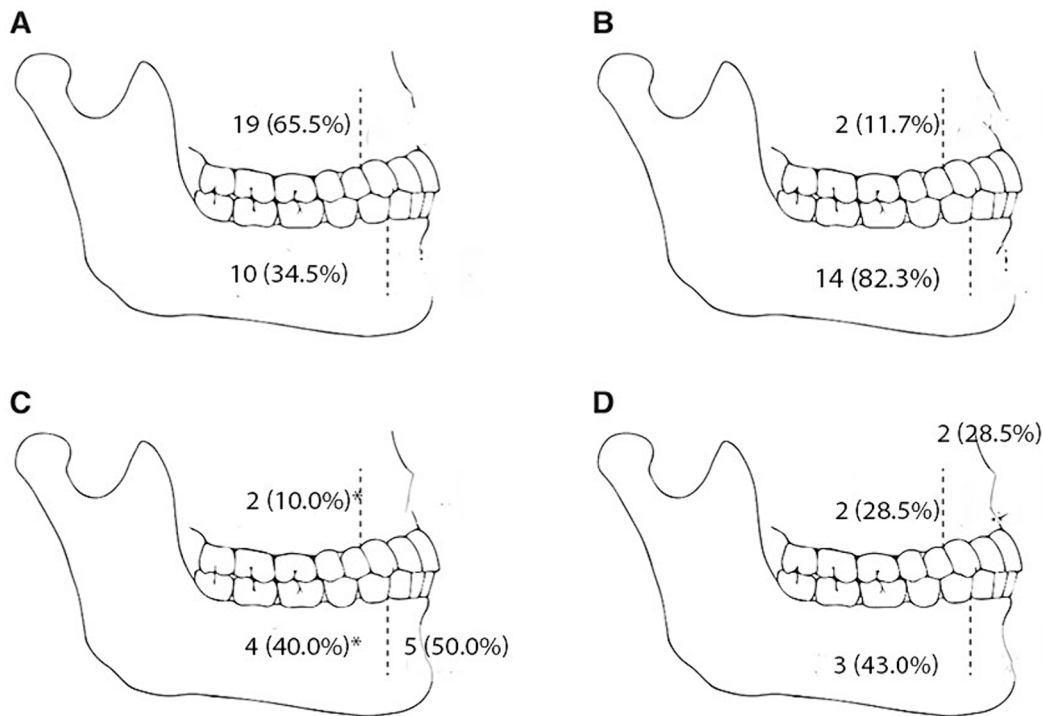* The age of four patients was not reported.

Fig. 2. Location distribution of BFOLs (A) Fibrous dysplasia, (B) Cemento-ossifying fibroma, (C) Cemento-osseous dysplasia (*one case of florid COD presented in both the maxilla and the mandible), (D) Aggressive ossifying fibroma.

Table 4
Summary of demographics and distribution of different types of COD.

Cemento-ossifying fibroma	Number of cases	Sex		Location				Complications (cases developed osteomyelitis
		Male	Female	Anterior Mandible	Posterior Mandible	Posterior maxilla	Bilateral maxilla and mandible	
Apical COD	5	0	5	5	0	0	0	0
Focal COD	3	0	3	0	2	1	0	1
Multifocal COD	2	0	2	0	1	0	1	1
Total	10	0	10	5	3	1	1	2

data from single oral pathology laboratories and may not represent the entire population. Therefore, the actual prevalence of BFOLs remains unclear.

Our study revealed that FD was the predominant type of BFOL (45.31 %). This finding is consistent with numerous studies, where FD has been reported to account for 36.7 %-56.1 % of all patients (Muwazi & Kamulegeya, 2015; Ogunsalu et al., 2001; Phattarataratip et al., 2014). Alternatively, studies by Soluk-Tekkesin M et al. (Soluk-Tekkesin et al., 2022) and Santos Netto et al. (de Noronha Santos Netto et al., 2013) found the predominant condition was COD, ranging from 49.0 % to 69.9 %. However, in our study, only 15.62 % of the patients had CODs. The lower percentage of CODs in our series may be since CODs are typically diagnosed radiographically, with biopsies often deemed unnecessary and therefore not recorded in oral pathology reports. Additionally, studies reporting higher frequencies of CODs, such as that by Soluk-Tekkesin M et al., (Soluk-Tekkesin et al., 2022) primarily used radiographic records to identify cases, which may explain the higher number of reported cases. AOF was the least common BFOL, accounting for 10.94 % of the cases, which is known to be a rare tumor. The demographic profile of our study cohort was consistent with previously reported data, characterized by a distinct female predilection and a frequent occurrence within the fourth decade of life (de Noronha Santos Netto et al., 2013; Muwazi & Kamulegeya, 2015; Soluk-Tekkesin et al., 2022).

The current study encountered limitations in the sample size for COD

and AOF, which hindered the substantial analysis of those conditions. In contrast, our study included 29 and 13 patients with FD and COF, respectively. FD displayed a minor female predisposition, whereas COF exhibited a pronounced inclination towards females, evidenced by a male-to-female ratio of 1:3.25. These findings were consistent with those reported by Alsharif et al. (Alsharif et al., 2009). Other studies have reported a stronger female predilection with notably higher ratios of 2.5:1 and 6.8:1 for FD and COF, respectively. Regarding age, FD patients were primarily identified in the 2nd and 3rd decades, which aligns with earlier observations (Alsharif et al., 2009; de Noronha Santos Netto et al., 2013; Muwazi & Kamulegeya, 2015; Phattarataratip et al., 2014; Worawongvasu & Songkampol, 2010). However, FD occurrences in Turkey exhibited a heightened prevalence in the 4th and 5th decades. (Soluk-Tekkesin et al., 2022). Conversely, COF patients were typically diagnosed in the 3rd and 4th decades, with different studies reporting a broader age range spanning the 2nd to 4th decades (Muwazi & Kamulegeya, 2015; Phattarataratip et al., 2014; Soluk-Tekkesin et al., 2022). Additionally, there was a notable predilection for FD in the maxilla, while COF was in the mandible in 80 % of the cases, consistent with the literature (de Noronha Santos Netto et al., 2013; Muwazi & Kamulegeya, 2015; Phattarataratip et al., 2014; Soluk-Tekkesin et al., 2022; Worawongvasu & Songkampol, 2010). Interestingly, the current study did not identify any patients with syndromic FDs. Only patients with FD showed recurrence, with a rate of 17.2 % during follow-up, which closely resembles previously documented recurrence rates (Ozsen et al.,

2018). The differences between the findings of the current study and previous research can be attributed to variations in study methodologies. These include differences in data sources, diagnostic criteria, demographic characteristics of study cohorts, and sample sizes. Varied data archives, from medical databases to pathological records, were utilized. Inconsistent diagnostic criteria, such as relying solely on histological slides or radiographic imaging, also contributed to differences. Additionally, demographic diversity and sample size discrepancies across studies affected the generalizability of outcomes.

FGC is an extremely uncommon autosomal dominant genetic condition, often affecting multiple jaw quadrants in the first two decades of life (Wang et al., 2017). While typically familial, sporadic cases have been reported (Noffke et al., 2012). Histologically, FGC is characterized by abnormal cementum-like material deposition within fibrous tissue, resembling COF. Despite its benign nature, FGC can lead to severe facial deformities, causing cosmetic and functional issues, if not managed properly (Wang et al., 2015). Its rarity is evident in the limited documented cases. It is noteworthy that our cohort is the first to identify this rare condition. Recent studies have identified unique mutations in the ANO5 gene in FGC, not seen in other BFOLs (Zhou et al., 2024).

This study provides the first comprehensive series on the demographic characteristics of BFOLs in Riyadh. However, the study's retrospective nature limits the accuracy of the data due to potential case attrition and inaccuracies. Since it's a single institution study, the findings may only partially represent the population, suggesting the need for multi-center collaborations to obtain accurate results. Additionally, an in-depth analysis of the genetic landscape of BFOLs is crucial to understanding their pathophysiology, which could improve the diagnosis, management, and prognosis.

5. Conclusion

Our findings provide valuable insights into the distribution of BFOLs aiding clinicians and researchers in the region. FD was most common, followed by COF. Future studies should delve into molecular aspects, clinical outcomes, and management in Saudi Arabia to enhance patient care.

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