### Ossifying Fibroma of the Jaws: Review of 57 Cases in Enugu and of Global Literature

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#### Abstract

**Background:** There are very few reports of the clinicopathological features of ossifying fibroma (OF) of the jaws in Enugu, South-east Nigeria. **Aims:** To study the prevalence and clinicopathological features of OF in Enugu. **Patients, Materials and Methods:** An eight-year retrospective study of patients with OF of the jaws was carried out in a tertiary hospital in Enugu, Nigeria. The clinical records, radiographs, histopathology reports, and slides of 87 patients with fibrous lesions, archived in the department of oral pathology and oral medicine were identified and examined. The cases diagnosed with OF by histological examination were retrieved and studied. The data were analysed using the descriptive statistics and presented in the form of frequency tables. The test for a statistical association was carried out using the Chi-square statistics. **Results:** There were 644 orofacial lesions and 13.5% (87) of these were fibro-osseous tumours. OF constituted 8.9% (57) of the orofacial lesions and 65.5% (57) of fibro-osseous tumors. The male-to-female ratio was 1:1.7. The overall mean age at tumour-onset was 24.1  $\pm$  13.1 years, (range: 5–60 years). The age group at which OF occurred most frequently (43.9%) was 11–20 years. The mandible was the most common site of occurrence, 64.9% (37), while the radiographic features were well-circumscribed opacity 24.6% (14), and mixed lucency–opacity, 22.8% (13). Conventional 54 (94.7%) and juvenile-psammamatoid 3 (5.3%) subtypes were identified. **Conclusion:** OF is the most prevalent fibro-osseous lesion, occurred mostly in the second decade and exhibits a lower mean age of onset in male patients.

Keywords: Fibro-osseous lesion, juvenile psammamatoid, orofacial lesion, ossifying fibroma

#### **INTRODUCTION**

Fibro-osseous lesions are a group of poorly defined lesions that include fibrous dysplasia, ossifying fibroma (OF),<sup>[1]</sup> and osseous dysplasia.<sup>[2]</sup> OF (70%) is the most common benign fibro-osseous neoplasm of the craniofacial region.<sup>[3]</sup> It is characterised by the replacement of the normal bone and marrow with a connective tissue matrix, and mineralisation with woven bone or acellular structures.<sup>[4,5]</sup>

OF was first described by Menzel in 1872 but was reported by Montgomery in 1927.<sup>[6]</sup> Various classifications have applied the term "OF,"<sup>[7]</sup> while in the 3<sup>rd</sup> edition of WHO classification 2005, the term "cementifying OF" was reduced to OF.<sup>[8]</sup> However, the 4<sup>th</sup> edition of the WHO classification 2017 and the most current, reclassified cement-OF as benign messenchymal odontogenic tumour, clearly distinguishing it from OFs that are classified under benign fibro- and chondro-osseous lesions.<sup>[9]</sup>

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Peripheral OF is the extraosseous variant while the intraosseous OF is subdivided into conventional and juvenile clinicopathological subtypes.<sup>[10]</sup> The term juvenile OF (JOF) is used to describe two distinct clinicopathological entities: Juvenile trabecular OF (JTOF) and juvenile psammamatoid OF (JPOF). Conventional OFs are usually slow-growing and generally seen in the third and fourth decades of life.<sup>[3,11,12]</sup> They predominantly affect females,<sup>[3,13,14]</sup> with a female:male ratio of 5:1.<sup>[15]</sup> OF presents with the expansion of the buccal and lingual cortices and may involve the inferior border of the mandible.<sup>[1]</sup> It is locally aggressive, with

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mandibular predilection, and often associated with significant esthetic and functional disturbances.<sup>[7,14]</sup>

Radiologically, OF appears as a well-circumscribed unilocular or multilocular radiolucencies or present as a mixed radiolucent-radiopaque mass with root resorption or displacement of adjacent teeth.<sup>[3,12]</sup> Central OF often presents with well-demarcated borders.

The precise global frequency of OF still poses a challenge due to the dearth of reported epidemiological studies and various terminologies that have been ascribed to the lesion.<sup>[6-8]</sup> There is a paucity of studies on the histopathology of OF from South-east Nigeria. This study will bridge the gap in knowledge and add to literature on the prevalence and clinicopathological features of OF in Enugu, Nigeria.

### **PATIENTS, MATERIALS AND METHODS**

This is a retrospective study of the clinicopathological features of patients diagnosed with OF in a tertiary hospital in Enugu, over an eight-year period. Patients' clinical records, histopathology reports, and slides in the department of oral and maxillofacial surgery were reviewed from January 2012 to December 2019. Inclusion Criteria: Patients included in the study were those diagnosed as OF by histopathology study, and those with additional information from radiographs and slides from existing formalin-fixed paraffin-embedded tissue blocks.

#### **Exclusion criteria**

Cases confirmed with OF by histology but with missing or damaged paraffin blocks or without adequate clinical records were excluded. Information collected includes age at presentation, sex, site of lesion, and histological diagnosis of the lesion. Other data collected were duration of the lesion and age at tumour onset obtained by subtracting the duration of the lesion from the age at presentation.

The age-at-onset of symptoms is different from the age-at-presentation in the clinic. The age-at-onset is when the patient became aware of the initial swelling or other associated symptoms before presentation to the clinic. The duration of the lesion is obtained from this point by the patient. The clinician obtains the age-at-onset by subtracting the duration stated by the patient from the age-at-presentation.

There was no interface with patients, but with archival documents, tissue blocks, and other records, and the Helsinki Declaration was followed for this investigation. An institutional approval was obtained for the study.

The data were analysed using the descriptive statistics and presented in the form of frequency tables. The test for a statistical association between the variables at a 95% confidence interval was carried out using the Chi-square statistics. The level of significance was set at 95% (P < 0.05). All statistical tests were done using IBM SPSS Statistics for Windows, version 24.0. (Armonk, New York:IBM Corp., United States).

### RESULTS

A total of 644 orofacial lesions were identified, out of which 13.5% (87) were fibro-osseous lesions. OF cases constituted 8.9% (57) of orofacial lesions and 65.5% (57) of fibro-osseous lesions, respectively. The overall mean age at tumour onset was  $24.05 \pm 13.14$  years. The range of ages at the onset of the lesion was 5-60 years. The mean duration of OF at presentation was  $3.4 \pm 3.5$  years, while the range of duration of lesions was from 0.2 months to 16 years. Table 1 shows the frequency of age group of patients at the onset of the tumour. The majority of OF (43.9%) occurred in the 11–20 years' age group.

Female patients constituted 63.2% (36) and 36.8% (21) were male, with a male-to-female ratio of 1:1.7. The mean age at onset for female patients was  $25.2 \pm 13.5$  years and  $22.1 \pm 12.6$  years for male patients.

The mandible was the site with the most frequent occurrence 64.9% (37) and followed by the maxilla 35.1% (20), while the mandible: maxilla ratio was 1.9:1. Table 2 shows the frequency distribution of OF on anatomic sides and association with jaw locations. The majority of lesions, 49.1% (28) were located on the right side. There was no significant association.

There was also no significant association side of the jaw affected by OF and the presence of ulceration (P = 0.24), nor with complaint of pain (P = 0.88), nor tooth mobility (P = 0.47).

Table 3 shows the frequency of radiographic patterns of OF and association with gender. The well-circumscribed opaque pattern of 24.6% (14) and mixed lucency – opacity of 22.8% (13) were most frequent. There was no shown significant statistic association with gender. Tooth mobility was not a frequent occurrence and was observed only in 7% (4) of the cases. Pain was observed in 7% (4) of cases

Table 1: Frequency of age group of the patients at onset of ossifying fibroma

Age groups (years)	Frequency (%)
1-10	5 (8.8)
11-20	25 (43.9)
21-30	13 (22.8)
31-40	8 (14.0)
41-50	2 (3.5)
51-60	4 (7.0)

## Table 2: Association of anatomic side of occurrence and jaw location

Side of jaw	Location		Total (%)	Р
	Mandible	Maxilla		
Right	18	10	28 (49.1)	0.62
Left	13	9	22 (38.6)	
Anterior	1	0	6 (10.5)	
Bilateral	5	1	1 (1.8)	
Total	37	20	57 (100)	

with all lesions located in the mandible, P = 0.127. Ulceration was observed in 3.5% (2) of the cases. Three (5.3%) of the lesions were recurrent conventional OF cases referred from other centres. Conventional OF was the most common type of OF, 94.7% (54) followed by juvenile-psammamatoid type, 5.3% (3).

Figure 1 shows the gross excision specimen of OF. The definitive diagnosis of OF was made based on the histological examination of incisional and excisional surgical specimens. Figure 2 shows a photomicrograph with moderately cellular fibrous stroma and broad variation in mineralisation of the bone. Often, woven bone, lamellar bone, or metaplastic bone with peripheral osteoblastic rimming was seen in some cases. The diagnosis of JPOF was made based on additional histologic identification of moderate to dense proliferation of spindle-shaped cells within which were ossicles, spherules, or psammoma-like calcifications. Other criteria for the diagnosis include predominant extragnathic craniofacial bone occurrence.<sup>[9]</sup> No diagnosis of JTOF was made in this series.

All the cases were treated by surgical excision and there has been no case of recurrence after variable years of follow-up of three – ten years.

### DISCUSSION

The precise global prevalence of OF is yet to be determined due to dearth of reported epidemiological studies and array of terminologies previously used for its description.<sup>[6,8]</sup> The prevalence of OF among fibro-osseous lesions in Enugu South-east Nigeria was 65.5% which is higher than the 51% previously reported in Enugu,<sup>[13]</sup> but similar to the 68.3% reported in Port-Harcourt, South-South Nigeria.<sup>[16]</sup> Lasisi *et al*.<sup>[17]</sup> reported a prevalence of 50.4% in Western Nigeria. In published studies from the regions of Nigeria, OF is currently recognised as the most common benign fibro-osseous lesion.<sup>[13,16,17]</sup>

A lower overall mean age at tumour onset of 24.1 years was observed in this study in contrast to the 30.9 years reported



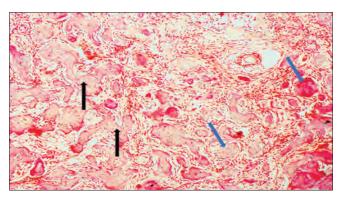
Figure 1: Gross specimen of ossifying fibroma. The tumour shelled out and felt gritty to cut

by Lasisi *et al.*<sup>[17]</sup> in Western Nigeria. Higher mean age was reported by some other studies from Nigeria and Europe.<sup>[2,17,18]</sup> It is well documented that the lesion occurs most frequently in patients below the age of 40 years.<sup>[6]</sup> This was the case in this study where 89.5% of patients were below 40 years of age. The lower mean age in this study could be because the estimation was based on the more representative age at which the tumour was noticed by the patient, instead of the age at clinical presentation. The variable periods of duration reported by patients before the clinical presentation could run into years and thereby unduly extend the estimated mean ages.

A systematic review reported a higher mean age of OF in Asia than in Africa, and the 20–39 years age group was most frequently affected globally.<sup>[6]</sup> This variation may be attributed to geographic, racial factors, and differences in diagnosis. The most affected age group in the present study was the 11–20 years' age group. However, studies in Nigeria including Iyogun *et al.*<sup>[16]</sup> observed that OF was predominantly in the 21–30 years age category, in agreement with previous studies by other authors.<sup>[17,18]</sup> Sule *et al.*<sup>[19]</sup> also reported the second and third decades of life. Other studies have also reported the more cases of OF in the third and four decades of life.<sup>[3,12,20]</sup> These higher variations of the most affected age group may be attributed to geographic and racial factors and estimations of age group based on the patient's age at tumour presentation.

## Table 3: Association of radiographic pattern of ossifying fibroma and gender (n=45)

Radiograph	Sex		Total,	Р
	Male	Female	n (%)	
Well-circumscribed opacity	4	10	14 (31.1)	0.36
Mixed-lucency opacity	7	6	13 (28.9)	
Unilocular radiolucency	1	8	9 (20.0)	
Multilocular radiolucency	1	3	4 (8.8)	
Diffuse haziness	1	3	4 (8.8)	
Peripheral thick, central less dense	0	1	1 (2.4)	
Total	14	31	45 (100.0)	



**Figure 2:** Photomicrograph of ossifying fibroma of the jaw (H and E,  $\times 100$ ). Moderately cellular fibrous stroma with irregularly-shaped woven bone trabeculae (black arrows) and globules of bone (blue arrows)

The mandible was more commonly affected which is in agreement with most published reports on the subject.<sup>[2,7,17,21]</sup> Moshy *et al.*<sup>[22]</sup> and El-Gehani *et al.*<sup>[23]</sup> in contrast reported a slight maxillary predilection, whereas Ogunsalu *et al.*<sup>[24]</sup> reported no predilection for any jaw site. The clinicohistological types of OF show different anatomical site preferences, while conventional OF has predilection for the mandible, JOF was more frequently located on the maxilla.<sup>[9]</sup> It is of interest that the majority (49.1%) of OF in this study were located on the right side of the jaw, but there was no significant association between the jaw side affected and the presence of ulceration (P = 0.24), nor complaint of pain (P = 0.88), nor tooth mobility (P = 0.47).

The predilection of OF has frequently favoured the female gender.<sup>[2,7,21]</sup> This observation was also made in this study and reported by other authors.<sup>[3,18,25,26]</sup> However, Bassey *et al.*,<sup>[27]</sup> Mohanty *et al.*,<sup>[28]</sup> and Hamner *et al.*<sup>[29]</sup> reported a male preference. On the contrary, Alsharif *et al.*<sup>[11]</sup> and Moshy *et al.*<sup>[22]</sup> reported no gender affinity as it was found equally in their series. The reason for the reported higher female prevalence is presently unexplained.

The prevalence of JPOF in this study was 5.3%. JPOF is more commonly reported than the trabecular variety and occurs predominantly in the sino-nasal and orbital bones. Tumours in these sites could result in nasal obstruction, epistaxis, proptosis, and visual impairments including blindness, ptosis, and papilledema.<sup>[13,15]</sup> The cases of JPOF in this series did not exhibit any of these remarkable symptoms and the radiographic features were consistent with those described in literature such as expansile and well-circumscribed radiolucent lesion.<sup>[15,30,31]</sup> There was no case of JTOF recorded during the period of the study.

Microscopic diagnosis of OF had relied on characteristic demonstration of encapsulation and mineralisation of lamellar bone and woven bone with peripheral osteoblastic rimming.<sup>[13-15]</sup> These features were observed in this study, although some of the cases occasionally exhibited the absence of osteoblastic rimming. However, combining the histologic with clinical and radiologic features always helped in reaching the diagnosis of OF.

Adjuvant diagnostic tools based on immunohistochemistry are useful in some cases with diagnostic challenges in differentiating OF from fibrous dysplasia. The quantification of immunoexpression of osteocalcin exclusively secreted by osteoblasts as a biomarker for bone formation process, and Runx2 has been suggested to be helpful in differentiating both lesions.<sup>[32-34]</sup> The osteocalcin was quantitatively more in fibrous dysplasia than in OF,<sup>[32,33]</sup> and both lesions differ in the composition of the bone matrix based on osteocalcin immunohistochemistry.<sup>[34]</sup>

The cases of JOF in this study were not histologically remarkable and posed no diagnostic challenges. These cases were similar to those described in other reports and characterised by a proliferation of spindle shaped-fibroblastic cells with the presence of small multiple cementum-like ossicles (psammomatoid bodies).<sup>[15,35,36]</sup> Other studies reported that multinucleated osteoclast-like giant cells (similarly seen in giant cell tumour, giant cell granuloma, and brown tumour of hyperparathyroidism) may be seen together with occasional normal mitotic figures, without cytologic atypia.<sup>[15,31]</sup> Some studies have also documented concurrent aneurysmal bone cyst or traumatic bone cyst formation with JPOF.<sup>[30,31]</sup> Fibrous dysplasia remains the most remarkable differential diagnosis of OF because it shares similar clinical, radiological, and histologic features though both are distinct lesions.<sup>[8]</sup>

OF is variably treated with excision, curettage and resection depending on the level of aggressiveness and history of recurrence.<sup>[37,38]</sup> The recurrent rate of cases received from peripheral hospitals in this study was low at 5.3%, there was no case of recurrence in this series after treatment. JOF could recur if local resection is incomplete.<sup>[30]</sup> Long-term follow-up is therefore necessary owing to its locally aggressive nature and high recurrent potentials, with rates of 30%–56% for JPOF.<sup>[36,39]</sup> Although malignant transformation is rare,<sup>[30]</sup> transformation of OF to osteosarcoma has been reported,<sup>[40,41]</sup> as well as sarcomatous transformations in long-term recurrent lesions.<sup>[42]</sup>

The significance of this study is in its being the second study of the subject in Enugu South East Nigeria and thereby contributing to the scant literature. This study presented a larger data set, covered a longer period of study and focused on the histopathology of OF.

This study limited it's focus to the clinicopathological features and prevalence of the lesion. The absence of any case of juvenile trabecular variant of OF among the reported tumours during the period of the study also limited the extent of the study. The translational value is the improvement in understanding the patterns of OF in Enugu, the awareness of it's earlier age of onset, rarity of the juvenile trabecular type, and absence of malignant transformation. Further studies are required on immunohistochemical studies to facilitate a more accurate diagnosis.

### CONCLUSION

OF is the most prevalent fibro-osseous lesion in this study and only conventional and juvenile-psammamatoid histologic variants were observed. It is the most common bone-related lesion in the second decade of life with a lower mean age of onset in this series.

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### **Conflicts of interest**

There are no conflicts of interest.

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