# CHARACTERISTIC RADIOLOGICAL AND HISTOLOGICAL PATTERNS OF JAW FIBROUS DYSPLASIA AND OSSIFYING FIBROMA.

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## CERTIFICATION

The undersigned certify that this dissertation entitled **Characteristic Radiological and Histopathological patterns of jaw fibrous dysplasia and ossifying fibroma** is the original work of Dr Jeremiah Moshy (DDS) who conducted the study during his postgraduate training in Oral and Maxillofacial Surgery between 2002-2007 at the University of Nairobi under our supervision.

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## DEDICATION

This dissertation is dedicated to my lovely wife Elizabeth, my sons, Goodluck and Michael for their encouragement and tolerance during my absence. They really endured my having been away and missed my love.

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## ACRONYMS

| | |
|---|---|
| DDS | Doctor of Dental Surgery |
| FD | Fibrous dysplasia |
| OF | Ossifying fibroma |
| COF | Cemento-ossifying fibroma |
| FOLs | Fibro-osseous lesions |
| Gsα | Alpha subunit of G-protein |
| CAMP | Cyclic adenosine monophosphate |
| COD | Cemento-osseous dysplasia. |
| PCD | Periapical cemental dysplasia. |
| FCOD | Florid cemento-osseous dysplasia. |
| Xq 26 | Long arm of chromosome 26. |
| KS | Keratin Sulphate. |
| C4s | Chondroitin-4-sulfate. |
| SPSS | Statistical package for social sciences. |
| UNDH | University of Nairobi Dental Teaching Hospital. |
| CF | Cementifying fibroma. |
| ACOF | Aggressive cemento-osseous dysplasia. |
| JAOF | Juvenile active ossifying fibroma. |
| FCD | Focal cemento-osseous dysplasia |

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ABSTRACT

**OBJECTIVE:** To document the characteristic histopathological and radiographical patterns of two common FOLs of the jaw bone: the ossifying fibroma (OF) and fibrous dysplasia (FD).

**Study Design:** A retrospective and prospective audit involving histopathologic and radiographic analysis of archival and any new material with full clinical record documentation.

**Setting:** University of Nairobi Dental Teaching Hospital (UNDH), School of Dental Sciences.

**Study Population:** All cases of fibro-osseous lesions diagnosed as FD and OF were retrieved from the files of the UNDH, Division of Oral Pathology and Oral Medicine over a 15-year period and new cases were included as they presented over a 6- month period.

**Methodology:**

The case reports of FOLs diagnosed as FD and OF were retrieved from the records of the UNDH, Division of Oral Pathology and Oral Medicine. Information regarding lesions diagnosed as FD and OF was analysed according to location, demographic and radiographic features. For all those cases identified, their paraffin embedded tissue blocks were retrieved from the archives. Slides were prepared from each block retrieved and stained according to the Haematoxylin and Eosin technique for histopathological verification. Available radiographs were analysed as to location of the lesions in the jaws and patterns of radiographic appearance. Data were entered into a computer software and statistical analysis done by using the SPSS Programme, version-10. Comparison between pathological parameters and final diagnosis was evaluated with the chi-square test.

**Results:**

Among the 149 cases of FOLs retrieved for evaluation, two cases affected both the maxilla and mandible and were removed from the evaluation. FD lesions constituted 40 (27.2 %) while 107 (72.8 %) were those of OF. The age ranged from 1-72 years and the median age was 20 years. The mean age was 24.19 years and the standard deviation was 13 years. The male to female ratio was 1: 1.9. Although a higher proportion of females were affected by OF compared to males, the differences were not statistically significant. FD was found to occur in the 1$^{st}$ to the 6$^{th}$ decades of life with the 2$^{nd}$ and 3$^{rd}$ decades mostly affected which was remarkably similar to the pattern of occurrence of OF.

# CHAPTER 1

## 1.1 INTRODUCTION AND LITERATURE REVIEW

### *INTRODUCTION*

The terms fibro-osteo-cemental (FOCLs) and fibro-osseous lesions (FOLs) are synonymous. These are lesions characterised by the replacement of normal bone by tissue composed of collagen fibres and fibroblasts that contain varying amounts of mineralized substance, which may be bony or cementum-like in appearance. The benign FOLs of the jaws share similarities in radiographic, clinical appearance, histogenesis and histopathology; and consequently pose difficulties in the classification and management [1]. Confusion with other osseous and soft tissue tumours may occur resulting into under-treatment or over-treatment. Several studies have been conducted in trying to characterise FOLs in the world literature using different methods.[2,3] Lan et al. studied 316 cases of FOLs and used histologic features to distinguish focal cemento-osseous dysplasia (FCOD) from cemento-ossifying fibroma (COF). However, they emphasized that the difference between FCOD and COF has its limits and clinical and radiographic information is important for accurate diagnosis. In the same study, clinical and radiological features were used to distinguish FCOD from COF and found that radiographic distinction of the two lesions had its limits, especially for small COF and unusually large examples of FCOD. They advocated an adequate biopsy with correlation of histopathologic features to reach an accurate diagnosis.

Waldron and Giansanti[4]in their review of sixty-five cases of FOLs used clinical, radiological and histologic features to characterise the diagnosis of fibrous dysplasia (FD) of the jaws and found that radiologic and clinical information coupled with histologic features were very important in reaching the correct diagnosis. The term FOLs is a generic designation of a group of jaw disorders (ranging from inflammatory to neoplastic) that microscopically exhibit a connective tissue matrix and islands/trabeculae of bone. Although the histological appearance and; frequently the clinical and radiographic features may be similar for many of these lesions, there is a wide range of biological behaviour and treatment. To date there are few well-established guidelines to help the surgeon[5]. A need for accurate classification is of paramount importance for proper management of the patient and for prediction of the outcome of the treatment.

## *REVIEW OF LITERATURE*

Maxillofacial FOLs consist of lesions that differ with the exception of FD to those found in the rest of the skeleton[6]. These lesions share similarities in their radiographic and clinical appearance, histogenesis and histopathology; and consequently pose difficulty in classification and treatment. Common histological features among these lesions include an active proliferation of fibroblasts, young and mature collagenous connective tissue, focal areas of mineralization which may resemble small cementicles and/or irregular bone trabeculae and multinucleated giant cells. A differential diagnosis of a benign FOL can, therefore, be made if clinical behaviour, radiographic features and haematologic changes are correlated with the histologic picture[1, 7, 8].

A bewildering number of diagnostic terms have been used for these lesions in the literature. Proper categorization requires good correlation of the history, clinical findings and histopathological appearance. Diagnosis based on histopathologic appearance alone has considerable limitations and often, the pathologists can be no more specific than a diagnosis of "benign fibro-osseous lesion" in the absence of adequate clinical and radiological data. However, with adequate biopsy or surgical specimen, most FOLs of the jaws can be reasonably assigned to one of the categories described by[8] Waldron which may include:

i. FD comprising the monostotic and polyostotic types.

ii. Fibro-osseous (cemental) lesions presumably arising in the periodontal ligament. These are categorized into four groups as follows:

- Periapical cemental dysplasia
- Localized fibro-osseous – cemental lesions (probably reactive in nature)
- Florid cemento-osseous dysplasia (Gigantiform Cementoma)
- Ossifying and cementifying fibroma

iii. Fibro-osseous neoplasms of uncertain or debatable relationship to those arising in the periodontal ligament which include:

- Cementoblastoma, osteoblastoma and osteoid osteoma.
- "juvenile active ossifying fibroma" and other so called "aggressive", "active"

  Ossifying/cementifying fibromas.

FD is a benign FOL presumably developmental in nature and characterised by the presence of fibrous connective tissue with a characteristic whorled pattern containing trabeculae of immature bone. The term FD was first suggested by [9]Linchestein as a designation for multiple bone lesions of the type described by [10]Albright et al. as osteitis fibrosa disseminata. [11]Lichenstein and Jaffe later expanded this concept and noted that an isolated (monostotic) form of the disease was considerably more common than the polyostotic form. Following Lichtenstein and Jaffe's[11] paper, the diagnosis of FD became very popular and was used almost all-inclusively as a diagnosis for benign bone lesions consisting of fibrous tissue and bone trabeculae. More recently there has been a trend to define FD by more exact clinical, radiologic and histologic criteria[6, 8, 12, 13]. However, the specific histopathologic criteria for diagnosing FD are still somewhat controversial. Most authorities consider the disease to be a non-neoplastic developmental (harmatomatous) lesion of bone. FD is a usually benign fibro-osseous abnormality of bone that may occur as monostotic, polyostotic, or craniofacial disease or as part of a syndrome. It is caused by a postzygotic, somatic mutation of the protein transcript of the "GNAS1" gene which encodes the α-subunit of the stimulatory G-protein. These activating mutations inhibit the instrinsic guanine triphosphatase activity of the adenylyl cyclase activity and a subsequent increase in intracellular cyclic adenoside monophosphate.

Mutations at position 201 of $G_s$ α in which arginine is replaced by cysteine or by histidine were found first in endocrine organs in patients with the McCune –Albright syndrome and then in monostotic and polyostotic FD in the FD-associated with the McCune-Albright Syndrome[14,15]. This mutation is thought to underlie the development of FD associated with a cellular retraction and deposition of abnormal bone matrix led by increased cyclic adenosine monophosphate (CAMP) formation. The clinical expression depends on the size of the cell mass and where in the cell mass the mutation occurs. In the postnatal life (during infancy, childhood or adult life) may result in monostotic FD. A mutation in a large cell mass during embryonic development is

likely to result in the polyostotic (Jaffe type) FD. A mutation in a small cell mass during embryonic development may result in the McCune-Albright Syndrome.

Several studies have been done evaluating the clinical features of FD of the jaws. According toWaldron[8], FD is seen with approximately equal frequency in males and females. Maxillary involvement is more common than mandibular; and the maxillary lesions not infrequently involve a group of contiguous bones separated by sutures including the maxilla, zygoma, sphenoid and occiput which in this sense are not strictly monostotic. A painless enlargement of the involved bone is the most common symptom. This is usually insidious in onset and often, the patient does not remember when the swelling first began. In keeping with the concept that FD is a developmental anomaly, a sizeable number of cases are detected during the first two decades of life. Other studies reported a painless enlargement of the involved bone as the only significant clinical finding and was almost invariably present. Pain and neurological manifestation plus mild temporomandibular joint symptoms also occurred. There is also insidious bone enlargement often resulting in facial asymmetry.

Intraorally, FD is reported to present with a smooth, often fusiform expansion of the alveolar ridge of the adjacent maxillary and mandibular bones. The covering mucosa is invariably normal in appearance, and ulceration is never seen or reported. Teeth are frequently present in the involved area and, although minor malposition is occasionally noted, marked mobility or exfoliation is not reported [4]. More than one-half of the patients are in the second and third decades of life. Swelling, which is pronounced in some cases, is a constant finding and few patients exhibit swelling only on intraoral examination and sometimes this is associated with malocclusion of the teeth. Most of the patients have facial asymmetry and a few have severe distortion of the facial contour.

With mandibular lesions, the swelling is found most often at the angle of the jaw while maxillary lesions cause bulging of the canine fossa or extreme prominence of the zygomatic process of the maxilla. Some extensive lesions are associated with ocular proptosis and exophthalmos. There are also changes of the contour of the affected bones, most often over the buccal and labial aspects of the jaws. Pain of a constant type occurrs and in some may exhibit abnormal cutaneous pigmentation. In Hong-Kong, Macdonald-Jankowski [16]reported that FD is more frequent in the maxilla of the oriental populations with swelling as the most frequent clinical finding.

Radiographic features of FD are extremely variable, ranging from cyst-like radiolucencies to dense, osteoblastic lesions. The radiographic appearance depends upon the amount of fibrous tissue that replaces normal bone and its distribution. Radiopacities occur when the fibrous elements have undergone calcification, the so called ground glass, "orange Peel" or finger- print appearance. Mostly the outline of the lesion is indistinct and tends to blend with the normal surrounding bone. Teeth are usually displaced and show loss of the lamina dura but seldom have root resorption. Other lesions may show the "sunray appearance" which is a rare radiographic appearance of FD[17]. Other studies reported a radiographic picture of buccolingual expansion of the involved bone, poorly defined borders of the lesion (lack of circumscription), ground glass appearance or the orange peel appearance, a mixed pattern of radiolucency showing irregular and heavy radiopaque foci (smoke pattern appearance), minor divergence of roots and displacement of teeth[4]. The ground glass appearance which is due to superimposition of a myriad of poorly calcified trabeculae, multilocularity or cystic lesions has also been reported. Other studies[18], have classified FD into six radiologic types with the cyst-like type being the most common. The most striking radiographic appearance was increased radiolucency. Other radiographic appearances of FD include the sclerotic, osteolytic and mixed types. These were classified according to density changes within the lesion[19].

A lesion which is accepted as FD shows a certain range of histologic features. The stroma is fibrous in nature but the cellularity and amount of collagen seem varied. The cellular stromal element is fibroblastic in type and the cytoplasm is difficult to define but the nucleus is vesicular or basophilic. Bone trabeculae usually tend to have large osteocytes within the lacuna. The margins of these bone trabeculae frequently showed an apparent streaming of collagen bundles into the surrounding stroma. No bone trabeculae have interconnection. There is also the woven type of bone. Osteoclasts are seen in most lesions, particularly in apposition to lamellar bone formation. Osteoblasts are occasionally seen but never prominent. There is evidence of cartilage, cyst formation or inflammatory cells[4]. In an analysis of 30 cases of FOLs in the Netherlands, eleven cases were FD and histologically showed a rather uniform appearance with a constant ratio of bone and fibrous tissue throughout the entire lesion and cellular mineralized particles were virtually absent[12]. FD has also been described histologically as a lesion which shows even islands of woven bone that fuse with the surrounding bone. However, FD occurring outside the maxillofacial bones comprised of lamellar bone and osteoblastic rimming [20].

FOLs demonstrate a broad spectrum of clinical and radiological findings, varying from small, asymptomatic, often multiple lesions about the apices of vital teeth to circumscribed expansile lesions that have the features of a benign neoplasm. From the histopathologic standpoint, however, the lesions are remarkably similar and consist of fibroblasts and collagen fibres with varying amounts of bone and; acellular, circumscribed, basophilic calcification often designated as cementum[8]. It is likely that these lesions originate from the elements of the periodontal ligament[4]. They appear to develop in intimate relationship with the roots of teeth or in the periapical region of edentulous parts of the jaw. Although larger lesions may be seen to extend into the antrum or ramus of the mandible, it is possible that they originated in tooth-bearing areas. From an actiologic stand point, this group of lesions also seems to be diverse. Some of them are possibly dysplastic others may be reactive while others are seemingly benign neoplasms[8].

### *Cemento-osseous Dysplasias (CODS)*

Lesions known as periapical cemental dysplasia (PCD) can be found in the tooth bearing jaw area and are similar to ossifying fibroma (OF) but without demarcation. These lesions may be focal (FCD), involving one or a few adjacent teeth and when they are more widely distributed they are named florid cemento-osseous dysplasia (FCOD). PCD should be distinguished from cementoblastoma, a lesion similar to osteoblastoma but connected with tooth apices[20]. Focally expressed CODS (PCD, FCOD, FCD and cementifying fibroma (CF) / OF) are two entities clinically recognized that are not easily differentiated histopathologically because of the lack of recognition of specific microscopic features[21]. PCD is also called periapical cementoma, periapical FD, periapical OF and appears to be reasonably well defined clinically and radiographically. The disease has a striking predilection for females and for persons of the black race. Multiple lesions frequently occur and the condition is detected primarily in the third, fourth and fifth decades of life.

Clinically it is an asymptomatic condition and is almost always detected during a routine radiographic examination. The lesion will initially appear as a well circumscribed radiolucent area at the apex of a tooth. At this stage the disease cannot be differentiated radiographically from an inflammatory periapical disease except that the involved tooth is vital. An older lesion will show central calcification and eventually may appear as a large dense central calcification with a relatively narrow radiolucent rim[8]. Histologically, an early radiolucent area shows a proliferating fibrous connective tissue with no evidence of inflammatory infiltrate. Small foci of

"cementum", osteoid or bone are almost invariably present. More advanced lesions show a greater proportion of mineralized cementum-like material or thick, sclerotic bone trabeculae. An admixture of bone and cementum is frequently present[8, 21].

FCOD exhibits widespread and extensive manifestation. These lesions appear well defined clinically and radiologically. Cases have been reported under a variety of diagnoses such as gigantiform cementoma, sclerosing osteitis, multiple enostoses and diffuse chronic sclerosing osteomyelitis[22]. While there is no question that true chronic sclerosing osteomyelitis does involve the jaws, the majority of cases reported under this designation can be more properly considered to be examples of FCOD[23]. The disease is almost exclusively seen in middle-aged and elderly black women. The lesions have the tendency of bilateral occurrence and often quite symmetrical in location. The most common presentation is one of bilateral, densely sclerotic lesions of the mandibular molar –premolar region, although accompanying bilateral or unilateral maxillary posterior involvement is not unusual[23]. The majority of patients are dentate at initial presentation. However, some partially edentulous patients show radiographic areas that are typical of PCD at the apices of the remaining vital lower anterior teeth. Histopathologically, the lesions consist of dense, sclerotic masses which have been interpreted as cementum[24]. The onset of symptoms is usually associated with exposure of densely sclerotic cemental masses to the oral environment from progressive alveolar atrophy under a denture, traumatically induced ulceration of the alveolar mucosa or tooth extraction or biopsy. All reasonable efforts should be made to preserve the teeth as in a number of instances; infection, pain and a protracted clinical course have followed elective extractions.

### *The Ossifying and Cementifying Fibroma*

The OF and CF of the jaws are well circumscribed, generally slow growing lesions which enlarge in an expansile manner. On occasion they may reach a very large size and result in considerable deformity. They are probably best classified as benign neoplasms[8]. Although the classification of the World Health Organization [22]and other authors [25] regard the CF as an odontogenic tumour and consider the OF separately as non-odontogenic neoplasms, this seems an arbitrary and unnecessary separation, as the clinical, radiologic and prognostic features of the lesions are identical [6, 8]. Because from a histopathologic standpoint, the calcified product in some cases consists almost entirely of amorphous, basophilic, usually rounded calcification commonly considered cementum; these lesions are often designated as CFs. Lesions in which the calcified

product consists almost entirely of woven or lamellar bone is usually designated OFs. Lesions containing an admixture of woven and lamellar bone are often designated COFs[8]. OF/CF may be encountered in patients over a wide age range, and the peak incidence is in the third and fourth decades[26-29]. The mandibular premolar –molar area is the most common location. However, the lesions have been found to be located in other craniofacial skeleton such as the maxillary sinus, sphenoid sinus, occipital bone, maxilla, nasal bones, ethmoidal sinus and the orbit[30-33]. Clinically the lesions most commonly present as a painless expansion of the jaw. They are asymptomatic and slow growing but in some cases may show aggressive behaviour. When noticeable swelling is revealed it causes mild deformity and migration of teeth may be an early clinical feature[2, 8, 27]. Radiologically the lesions are well circumscribed and tend to show a sharply defined border. They may be completely radiolucent or show variable calcified components. Large mandibualr lesions may cause a characteristic thinning and downward "bowing" of the inferior border. Teeth adjacent to or involved in the lesions may be displaced but root resorption is not associated with this tumour. Some may show mixed density: radiolucent and radiopaque. Other studies have reported cystic radiolucent and ground glass appearances[8, 21, 34, 35].

There is no absolute histopathological distinction between bone and cementum since cementum-like areas of calcification are seen in FOLs of all membrane bones. Hence the distinction between OF and CF should be discontinued[36]. Histopathologically, these lesions are characterised by an equal amount of calcified material and a fibroblastic stroma. The calcified structures consist of both separate and retform bony trabeculae with a prominent osteoblastic rimming and occasional osteoblasts. Rounded or lobulated cementum-like bodies may be scattered throughout the lesions which sometimes may be a major component such as in CFs. The connective tissue consists of sheets of spindle fibroblastic or stellate cells with a focal area of storiform pattern. Other lesions may be composed mainly of mature bone, regularly aligned bone and intermingled fibrous tissue[37-39].

### *Non-Specific FOLs*

Fibro-osseous neoplasms of uncertain relationship to those arising in the periodontal ligament include several well-recognized neoplasms that are usually not considered to be FOLs of the jaws. However, they have sufficiently overlapping histopathologic features with FOLs arising in the periodontal ligament. These lesions, sometimes designated as juvenile (active, aggressive) OF also bear an ill-defined relationship to the more usual types of OF/CFs[8]. Osteoblastoma and osteoid osteoma are recognized neoplasmas in the extragnathic skeleton and have occasionally been reported in the jaws. There is a wide agreement that osteoblastoma and osteoid osteoma are closely related lesions and are separated only on the basis of their clinical and radiologic characteristics[40]. The radiographic findings in osteoblastoma of the jaws and the remainder of the skeleton are quite inconsistent and showing varying combinations of radiolucency and calcification that sometimes are indistinguishable from the typical OF/CF. Histopathologically, osteoblastomas can show a range of features, but most typically they have a highly vascularised stroma containing irregular frequently anastomosing trabeculae of osteoid and immature bone with varying degrees of calcification.

The osteoid trabeculae are surrounded by prominent, plump osteoblasts, and similar osteoblastic-like cells are conspicuous in the inter-trabecular spaces. Varying numbers of multinucleated giant cells may also be present. Although the histopathologic findings in the usual osteoblastoma are fairly distinctive, they have enough overlapping features with some OFs so that the designation of a given lesion as an osteoblastoma or OF may be controversial. Therefore, in the list of differential diagnosis, the CF or OF should also be taken into account[41]. Cementoblastoma has been recognized as a specific tumour of odontogenic origin and does present rather distinctive radiologic features. It shows remarkably similar histopathologic features to some osteoblastomas.

Juvenile active ossifying fibroma (JAOF) and other so called "aggressive" or active ossifying/cementifying fibromas occasionally appear in the literature. Unfortunately both the terms and the clinical and histopathologic criteria for separation of these lesions from the more common OF/CFs are ill-defined [8]. JAOF is most often seen in the maxilla and most patients are in the first or second decades of life. The diagnosis of JAOF, OF or CF has also been applied to tumours involving the bones of the skull in locations apart from the maxilla[42, 43]. Histopathologically the lesion is dominated by numerous small round, "Psammoma-like ossicles embedded in a cellular benign spindle cell stroma[44].

Aggressive cemento-ossifying fibroma (AC-OF) is the most aggressive tumour of all cementum-containing neoplasms. The unique site of origin is thought to be the result of ectopic periodontal membrane or of a primitive mesenchymal cell nest[45]. These lesions are radiologically well circumscribed, but the margins are poorly defined. When located in the fronto- ethmoidal region, the tumours encroach on the medial wall of the orbit, causing proptosis and exopthalmos. They have high recurrence after resection and have been diagnosed as OF, CF, COF or FD[46].

A review of the literature shows the difficulty in establishing a definitive diagnosis of FOLs through any single diagnostic modality. Adjunctive radiographic and nuclear medicine diagnostic aids were utilized as well as clinical, laboratory and histopathological studies in resolving the diagnostic difficulties posed by this large group of lesions. [47]Sawyer et al. in their study confirmed that there is a possibility of histopathological differentiation between OF and monotostotic FD with craniofacial sites. Some studies have used chromosomal breakpoints at bands Xq 26 and 2q33 to characterise FOLs[48]. Others have shown that the pathogenesis of FD results from post-zygotic activating mutation of the GNAS1 gene. Mutation of the $\alpha$ – subunit of signal-transducing G-proteins ($G_s\alpha$ mutations at the Arg 201 codon) is quite useful for distinguishing from other FOLs[14].

A recent study in the surgical pathology literature has used the immunoreactivities for keratin sulfate (KS) and chondroitin-4-sulfate (C4s), glycosaminoglycans of the histopathological samples obtained from mandibles of the patients with FOLs to differentiate CF from other FOLs[49]. This means that immunohistochemical analysis for keratin sulphate (KS) and chondroitin-4-sulfate could be used as a marker for differentiating FOLs. Despite all these efforts there is still shortfall in differentiation and diagnosis of FOLs.

## *Histopathological and Radiological Techniques*

A number of standard histopathological methods are available for the investigation of calcified tissues. These include electron microscopy, histochemical techniques and immunohistochemical methods. While electron microscopy provides ultrastructural cellular structure by scanning and transmission modes and utilized whenever fine structural[50, 51, 52] details of cells and tissue are required, histochemical methods bind to specific cellular and tissue proteins and stain them. Haematoxylin and Eosin is a universal stain used for staining tissues.

Specific histochemical stains for this purpose include Vonkossa, Gomori's silver impregnation and periodic acid Schiff[23, 36, 51, 53]. Immunohistochemical methods are relatively new and utilize monoclonal antibodies which detect and bind to tissue specific receptors. The resulting antigen-antibody complexes are detected by colour changing compounds indicating positive staining as in the immunoperoxidase techniques[44, 50, 52, 54]. Burkhardt[55] used a combination of these techniques in an extensive investigation of FOCLs and provided evidence for a dental origin. The immunohistochemical technique is now widely used and provides a relatively more accurate diagnossis than the conventional histochemical techniques. However, the nature and histopathological pattern of FOCLs is so varied that mixed types of calcified tissue seem to be frequent (osteo-cemental) and a distinction often impossible. Ultrastructural techniques include : S100[52,55,56], Vimentin [50,51] and Keratan sulphate[49].

Radiographic techniques used to investigate FOLs of the jaw bones include conventional plain film radiographs and CT-scans. Plain radiographs will display radiolucent, radiopacity, mixed radiopacity and radiolucency. They will also show whether the lesion is poorly defined or demarcated. CT-scans determine the extent, specific dimensions and radiodensity of these lesions. CT-images can display the range of opacifications observed on plain radiographs but the radiodensity observed is a function of windowing. The bone window displays densities generally observed in conventional radiographs whereas the soft tissue window generally displays mineralized tissue as white[26]. Radiographs usually define the limits and characteristics of the gross pathological conditions. The appearance varies according to the degree of maturation which determines the degree of opacification. Therefore, combined radiological and histopathological features are important in diagnosing these lesions. The aim of this study was to document the characteristic radiological and histopathological patterns of FD and OF of the jaw bones.

## 1.2 JUSTIFICATION OF THE STUDY

Differentiation of FOLs by histopathological and radiological evaluation is often difficult. Histopathologically, the features of these bone lesions appear quite similar and their precise nature remains controversial. These lesions also may represent different stages in the evolution of a single disease process. Some of the lesions are very aggressive, for example the aggressive ossifying fibromas (AOFs) and the unique histopathologic appearance of this particular lesion demonstrate a close relationship to a well-differentiated osteosarcoma. Hence the need to advocate for more definitive microscopic criteria to properly identify such lesions as either benign or malignant. Other lesions in this group are potentially massive in size and can result in considerable morbidity. Correct diagnosis of these lesions is important since some require no treatment unless secondary afflictions such as osteomyelitis develop while others require aggressive treatment since they have higher recurrence rates following treatment. In addition, confusion with other osseous and soft tissue tumours may occur resulting in too limited or too aggressive management. This necessitates accurate classification and diagnosis in order to help direct the correct treatment and predict the outcome.

## 1.3 Broad objective

To document the characteristic histopathological and radiolographical patterns of the two common FOLs of the jaw bones: the OF and FD.

## 1.4 Specific objectives

1. To determine the demographic patterns of occurrence of FD and OF of the jaw bones.
2. To determine the radiographic characteristics of FD and OF of the jaw bones.
3. To determine the histopathological characteristics of FD and OF utilizing the Haematoxylin & Eosin staining technique.
4. To compare and contrast the radiographic and histopathologic characteristics of FD and OF of the jaw bones.

## CHAPTER 2

## 2.0 MATERIAL AND METHOD

This study was approved by the Ethics, Research and Standards Committee of the Kenyatta National Hospital and the University of Nairobi – Approval No.98/6/2005 (Appendix 5.7).

### 2.1 Study design:

A retrospective and prospective audit involving histopathologic and radiographic analysis of archival and any new available material with full clinical record documentation

### 2.2 Study instruments:

The instruments for this study included the following:

- Files for surgical cases with the diagnosis of FD and OF actively treated at the UNDH over a period of 15 years (Jan.1991-Jan.2006); and any other new material obtained by incisional or excisional surgical procedures (Dec 2005- Jun 2006).
- Plain radiographs or CT-scans of the cases of FD and OF traced from these files for a period of 15 years in addition to those acquired from new cases. They were analysed by means of a viewing box in a dimly lit environment and findings recorded in specially designed charts.
- Paraffin-embedded tissue blocks of FD and OF.
- Slides prepared from the tissue blocks of FD and OF. These were studied under a light microscope (x 100 original magnification).

### 2.3 Area of Study:

This was carried out at the School of Dental Sciences, Division of Oral Pathology and Oral Medicine.

### 2.4 Variables:

The variables included the types of FOL affecting the jaws, location, clinical and radiologic features in addition to the histopathological variants.

## 2.5 Material/Population:

All archival tissue specimens of FOLs diagnosed as FD and OF were retrieved from the laboratory archives of the UNDH, Division of Oral Pathology and Oral Medicine over a 15-year period. New cases were included as they presented over a 6-month period. Considering the infrequency of occurrence of these lesions and the small number of cases reported in the literature, all the cases retrieved formed the sample of this study.

## 2.6 Methods:

The relevant case reports of patients histopathologically diagnosed to have had FOLs at the UNDH, Division of Oral Pathology and Oral Medicine were retrieved and reviewed. Information regarding the type of FOL, location, clinical features, demographic and radiographic data was documented for analysis.

## 2.7 Histopathological analysis:

For cases retrieved from the filed reports with a diagnosis of OF and FD, paraffin embedded tissue blocks were retrieved from the archives of the histopathology unit. Slides were prepared from each block retrieved and stained by the Haematoxylin and Eosin technique for histopathological evaluation. This was done under the supervision of a histopathologist experienced in oral and maxillofacial pathology. Histopathological slides of each case were analysed on the basis of selected pathologic parameters that consisted of three categories thus: gross features, shape and arrangement of calcified components, cellularity and pattern of non-calcified components. The selected pathologic parameters under each category were as follows:

**Gross features**

- Single or large enucleated pieces
- Multiple curettage fragments
- Capsule

**Calcified Components**

- Thick curvilinear trabeculae
- Irregular cementoid masses
- Separate bony trabeculae
- Metaplastic woven bone in a fibrous stroma
- Variable amounts of lamella bone
- Bone trabeculae with large osteocytes within the lacuna
- Osteoblastic rimming

**Non-calcified components**

- Storiform pattern
- Giant cells
- Free haemorrhage
- Dense collagen
- Loose collagen

## 2.8 Radiographic evaluation:

Available radiographs were analysed as to the location of the lesion in the jaws (maxilla and mandible). The radiographic patterns of the lesions and status of the margins surrounding the lesion was determined. The radiographic patterns of the lesions were classified into radiologic types according to the appearance of their matrices as follows:

- Radiolucency.
- Radiopacity.
- Mixed change of radiolucency and radiopacity.

- Ground glass appearance [alternating areas of radiopacity and lucency].
- Diffuse sclerotic [homogenous dense area of involvement with demarcation of the lesion from normal area of bone not clear].
- Cystic radiolucency [in this type, radiolucency would be the most striking radiographic appearance].
- Others [displacement of teeth, loss of lamina dura and bone expansion].

The status of the margins surrounding the lesion were evaluated as to whether they were defined margins with sclerotic borders, defined margins without sclerotic borders and ill-defined borders.

### 2.9 Reproducibility:

To reduce intraobserver and interobserver variation of the histopathologic assessments, five slides from each of the two lesions (OF and FD) were prepared and examined by the investigator for the histopathologic characteristics common to them. The same slides were reviewed by a supervisor who was a specialist in histopathology. The results of the two were compared to get a control for histopathologic features for the two lesions. In addition, each available radiograph was examined by the investigator for radiographic features common to the two lesions and then reviewed by a supervisor who was a specialist radiologist. In both examinations if there was at least 80% agreement, reproducibility had been achieved.

### 2.10 Subjectivity:

To minimize subjectivity, the evaluation was conducted independently without the knowledge of the histopathology or final diagnosis.

### 2.11 Analysis:

Analysis was done using the SPSS (1997) version 10. Univariate comparisons of the association between the histopathological parameters and final diagnosis were evaluated with the Chi-squared test.

## CHAPTER 3

# 3.0 RESULTS

## 3.1 Demographic Analysis

Out of the 2649 surgical files reviewed during the 15- year period (Jan.1991-Jan.2006) and subsequent new cases seen over 6 months (Dec.2005-May.2006), a total of 149 cases of FD and OF/COF were found. Two cases were omitted in the analysis because they affected both the maxilla and mandible. Out of the remaining (147 cases), 27.2% of the cases had been diagnosed as FD and 107(72.8%) as OF. Patients' ages ranged from 1 to 72 years with a median of 20 years. The mean age was 24.19 years (STD ' 13. 3 years). Females comprised the majority (65.3%) of the patients at a ratio of 1.9: 1. Although a higher proportion of females was affected by OF compared to males the difference was not statistically significant (P– 0.108) (Fig.1).

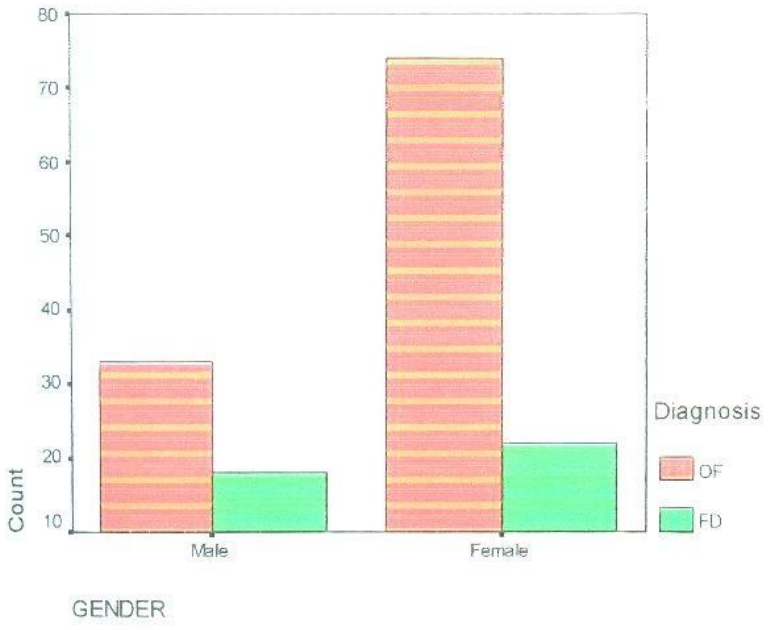



**Fig.1.** Distribution **of lesions according to gender.**

**Distribution of lesions according to age group.**

FD was found to occur in the 1st to 6th decades of life with the 2nd and 3rd decades mostly affected. The pattern of occurrence OF was essentially similar (Fig.2).

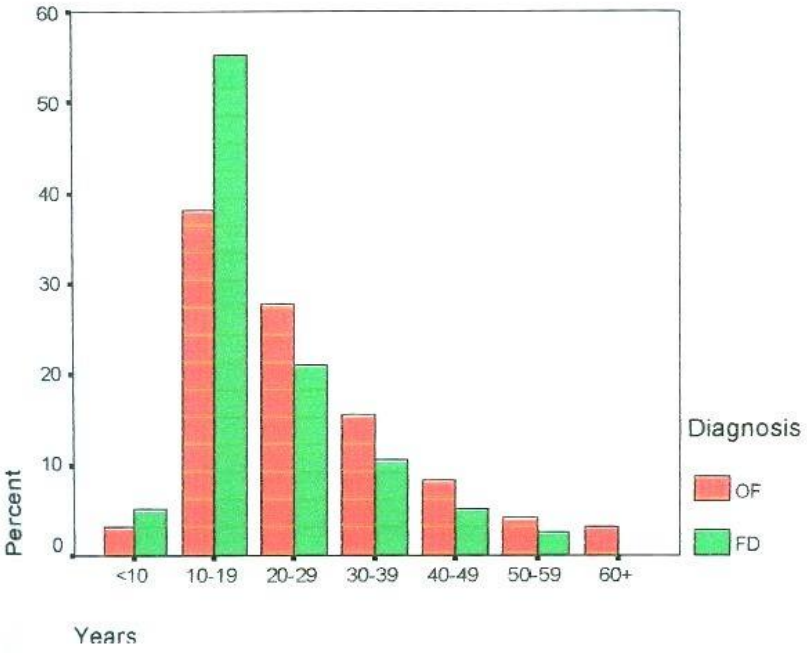



**Fig.2. Distribution of the lesions according to age group.**

**Distribution of lesions according to location in the jaws.**

Seventy one cases of OF and FD were located in the mandible while sixty six cases were located in the maxilla. One case of FD was located in both jaws. Of those located in the mandible alone 60 (84.5%) were OF while 11 (15.5%) were FD. While among those located in the maxilla, 41 (62.1%) were OF and 25 (37.9%) were FD.Compared to the mandible, more of the FDs were located in the maxilla (Table1). Analysis of the 72 cases which had specific sides recorded (left or right) showed that the left side of the maxilla was the most affected by both lesions. FD was observed to occur mostly in the left maxilla followed by the right mandible and the left maxilla; and the right mandible (Fig.3). However, these results were not statistically significant (p= 0.351).

**Table 1. Distribution of lesions according to location in the jaws**

| | Diagnosis | | Total | Test |
|---|---|---|---|---|
| | OF | FD | | |
| Mandible | 60 (84.5%) | 11 (15.5%) | 71(100%) | |
| Maxilla | 41 (62.1%) | 25 (37.9%) | 66(100%) | $\chi$=8.848 |
| **TOTAL** | **101 (73.7%)** | **36 (26.3%)** | 137(100%) | p= 0.003* |

* Statistically significant p<0.05

* 1 case was located in both maxilla and mandible
* 11 cases has no location recorded

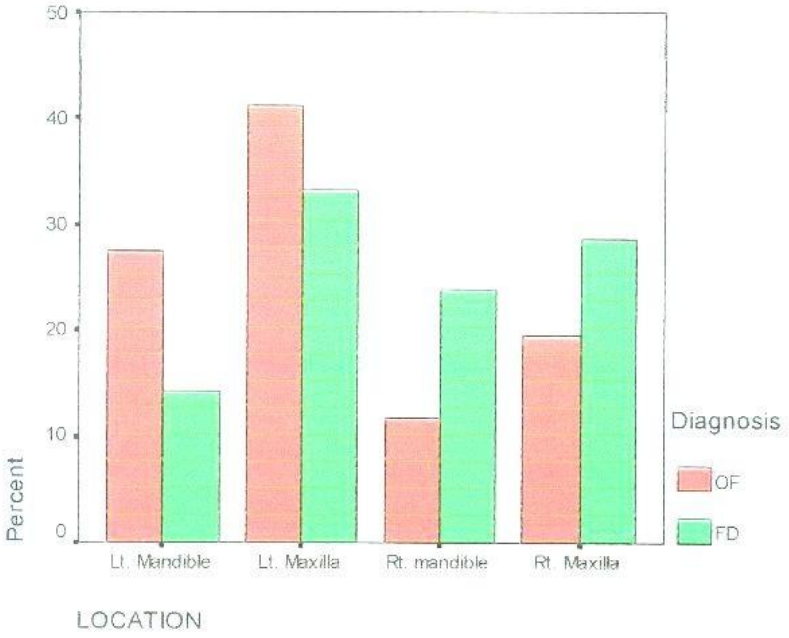



**Fig.3. Pattern of jaw site occurrence of the FD and OF lesions**

## 3.2 Radiologic Evaluation

Thirty eight radiographic records of OF and FD were available for evaluation. OF comprised of 26 radiographs while 12 were those of FD. OF yielded five radiographic appearances including the mixed type 12; radio-opaque 5, diffuse sclerotic 1 and ground glass appearance 4. FD depicted three radiographic appearances including the mixed type 3, the diffuse sclerotic type 4 and ground glass pattern 5. The results were statistically significant at p= 0.012 (Table2). Evaluation of the extent of lesions showed that OF presented with well defined borders with sclerotic margins (100%), well defined borders without sclerotic margins (81.8%), ill- defined margins (41.2%). FD presented with well defined borders without sclerotic margins (18.2%) and ill -defined margins (58.8%). These findings were statistically significant at p= 0.003 (Fig.4). Other radiological features observed in both lesions were bone expansion 25 (45.4%) for OF,

12(21.8%) for FD; loss of lamina dura 3(5.5%) for OF and 1 (1.8%) for FD; root resorption 5(9.1%) for OF and none for FD; tooth displacement 5(9.1%) for OF and 4(7.3%) for FD.

Table 2 and Figure 4 summarize the radiological features characterizing FD and OF. Plain x-rays (PA-views, OPG, Occlusal views, Waters' views) and few CT-scans were used for analysis. Notable overlapping of many of the features was demonstrated.

**Table 2. Radiological features characterizing OF and FD.**

| Radiological features | OF | FD | P VALUE Chi square |
|---|---|---|---|
| Radiological appearance | | | |
| Mixed type | 12(31.6%) | 3(7.9%) | $\chi$=12.91 |
| Radiopaque | 5(13.2%) | 0(0%) | |
| Radiolucent | 4(10.5%) | 0(0%) | 0.012* |
| Diffuse sclerotic | 1(2.6%) | 4(10.5%) | |
| Ground glass appearance | 4(10.5%) | 5(13.2%) | |
| Bone expansion | 25(45.4%) | 12(21.8%) | 0.684[a] |
| Loss of lamina dura | 3(5.5%) | 1(1.8%) | 0.625[a] |
| Root resorption | 5(9.1%) | 0(0%) | 0.131[a] |
| Teeth displacement | 5(9.1%) | 4(7.3%) | 0.289[a] |

* Statistically significant $p<0.05$

a: Chi-square test could not be performed so Fisher exact test was done.

* Even if the Chi-square test was significant, the small number of X-rays makes the test inconclusive.

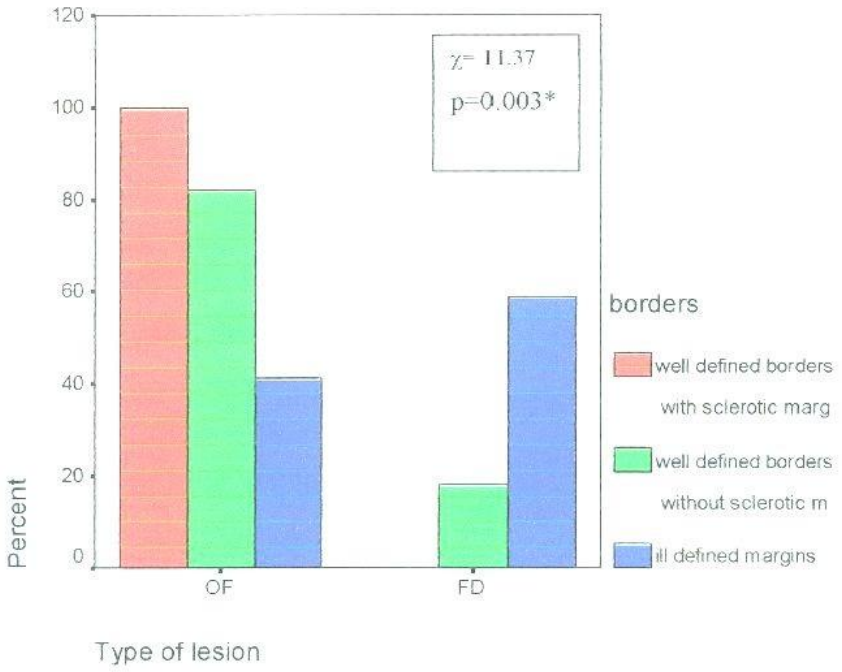



**Fig.4. Radiological appearance of borders in OF and FD**

Figures 5 to 7 demonstrate the diverse radiologic appearances of FD and OF. Note the changes that that may evolve over time with OF particularly.

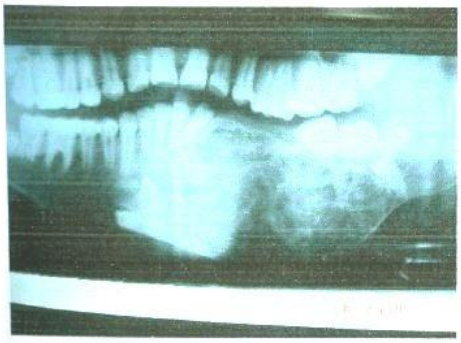


**Fig.5 A. Shows the sclerosing diffuse Ill-defined margins typical of FD**




**Fig.5 B. The ground glass appearance Consistent with FD.**

A. B.

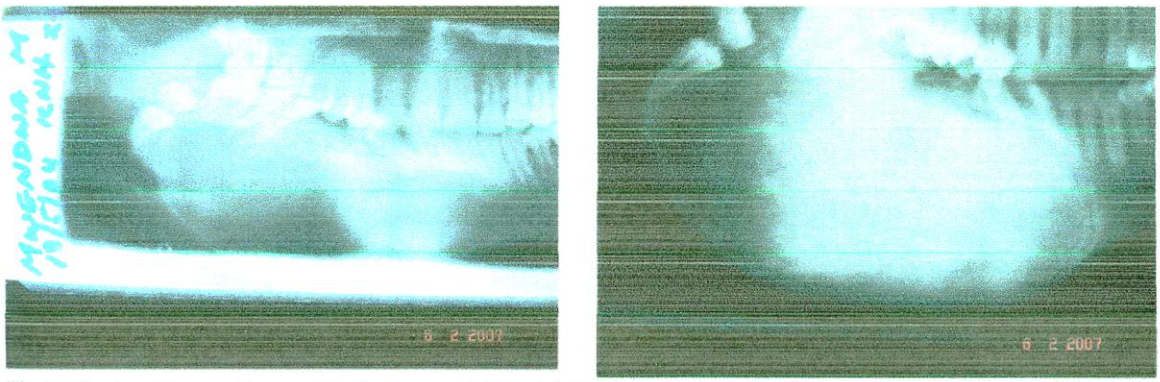


Fig.6. Contrasting radiographic features of OF at initial presentation (A) and one year later (B).

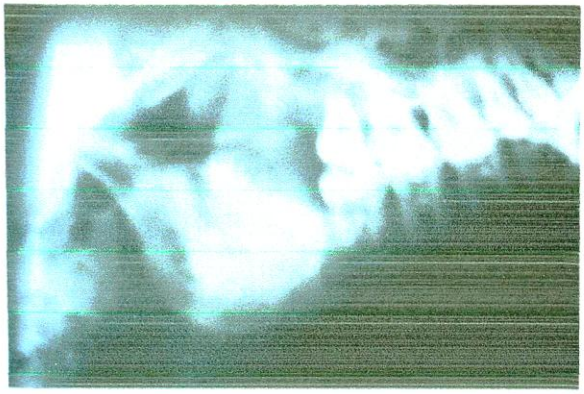


**Fig.7. Depicts a homogeneous opacity with a Smooth Outline conforming to appearance in OF.**

## 3.3. Histopathologic Characterisation of FD and OF

Of the cases of FD and OF analysed histopathologicaly, almost all FD (93%) cases were composed of multiple small fragments of tissue with free haemorrhage. Bone trabeculae with large osteocytes within the lacunae were present in all cases of FD while irregular cementoid masses comprised 33%. OF comprised more of the irregular cementoid masses (68%) compared to FD (33.3%). Other features found in OF included bone trabeculae with large osteocytes within the lacunae (56%), free haemorrhage (56%), multiple curettage fragments (48%) and thick curvilinear trabeculae (24%). All these features were statistically significant for FD and OF (Table3).

**Table 3. Proportions of histopathological components demonstrated in FD and OF**

| Features | FD n = 15 | OF n = 25 | p-value * Chi-square |
|---|---|---|---|
| **Gross features** | | | |
| • Multiple curettage fragments. | 93.3 % | 48.0 % | 0.004 |
| **Calcified components.** | | | |
| • Thick curvilinear trabeculae | 60.0% | 24.0 % | 0.023 |
| • Irregular cementoid masses | 33.3% | 68.0 % | 0.033 |
| • Bone trabeculae with large osteocytes within lacuna. | 100.0 % | 56.0 % | 0.003 |
| **Non-calcified components.** | | | |
| • Free haemorrhage. | 93.3 % | 56.0 % | 0.013 |

*** P < 0.05 was considered significant.**

There were remarkable common features observed in both FD and OF including metaplastic woven bone in a fibrous stroma which was a constant feature in both lesions. Other common features for FD and OF included separate bony trabeculae, variable amounts of lamella bone, single or large enucleated pieces, dense collagen and loose collagen (Table 4).

**Table 4.Similarities in Histological features in FD and OF**

| Features | FD n = 15 | OF n= 25 | P-value * Chi-square |
|---|---|---|---|
| Gross features. | | | |
| • Single or large enucleated pieces. | 6.7 % | 32.0 % | 0.063 |
| Calcified components. | | | |
| • Separate bony trabeculae | 66.7 % | 80.0 % | 0.346 |
| • Metaplastic woven bone in fibrous stroma | 100.0 % | 100.0 % | a |
| • Variable amounts of lamella bone. | 33.3 % | 8.0 % | 0.081 |
| Non-calcified components. | | | |
| • Storiform pattern. | 33.3 % | 52.0 % | 0.251 |
| • Dense collagen. | 26.7 % | 24.0 % | 0.850 |
| • Loose collagen. | 73.3 % | 76.0 % | 0.850 |

*** P < 0.05 was considered significant**

The study also revealed some histopathological features which were depicted in only FD or OF. Thus, 12 % of the OF cases had osteoblastic rimming while none was elicited in all the FD cases. Giant cells were demonstrated in 13% of the FD cases but none were present among all the OF specimens. Further more, 20% of the OF lesions had a demonstrable capsule while none of the lesions in the FD group showed any evidence of encapsulation. Figures 8 to 12 demonstrate the various radiologic and histopathologic features in FD and OF.

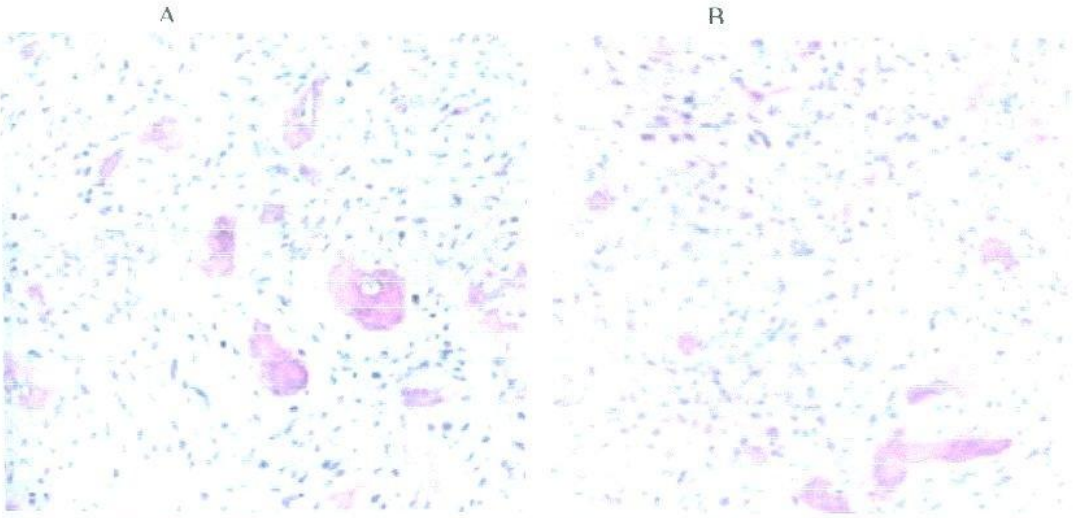



**Fig.8. Contrasting histopathologic appearance of OF (A) and FD (B) depicts more calcified components in OF (Original magnification x100, H&E).**

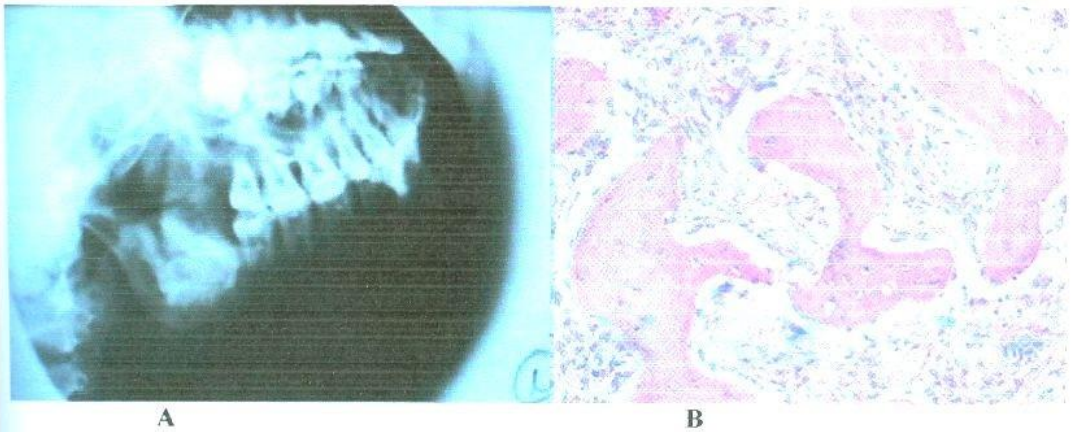
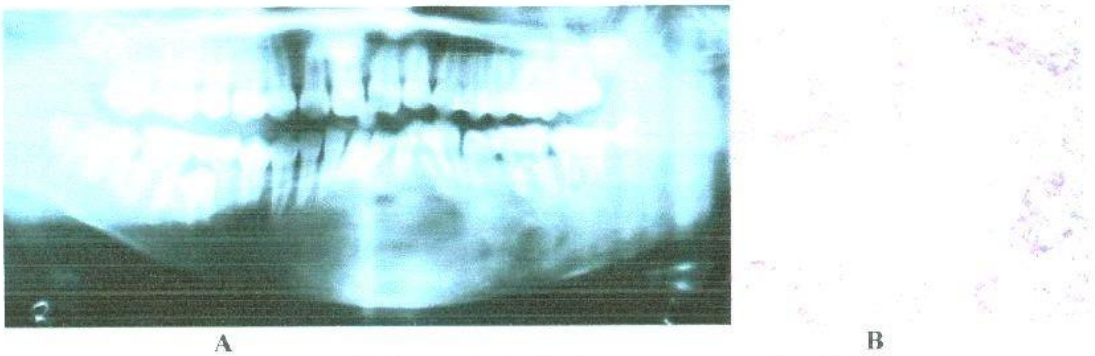
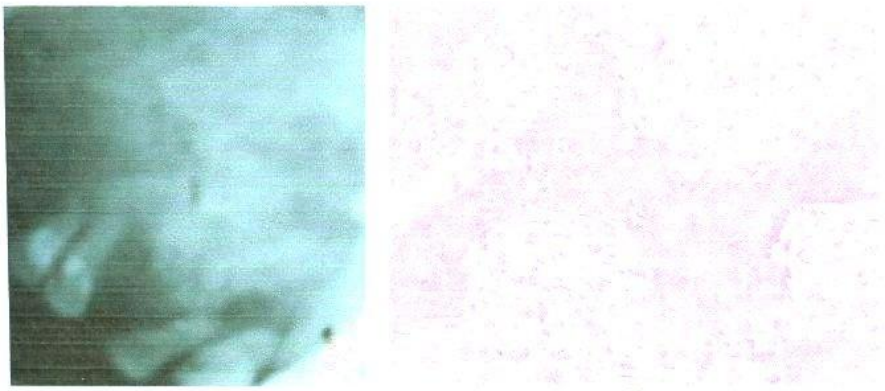



**Fig.9.Homogenous opacity appearance of OF (A) with increased formation of calcified components with the histopathologic features (B) resembling those in the FD with the ground glass appearance (Original magnification x 400, H&E).**



A B

**FIG.10. Radiographic (A) and Histopathologic (B) appearance of early FD. Histopathologically it is more cellular with increased collagen fibres while radiographically presents radiolucency appearance with ill-defined margins (Original magnification x 400, H& E).**



A B

**Fig.11.Shows ground glass presentation of FD (A) which histopathologically (B) depicts the formation of calcified components (Original magnification x 400, H&E).**

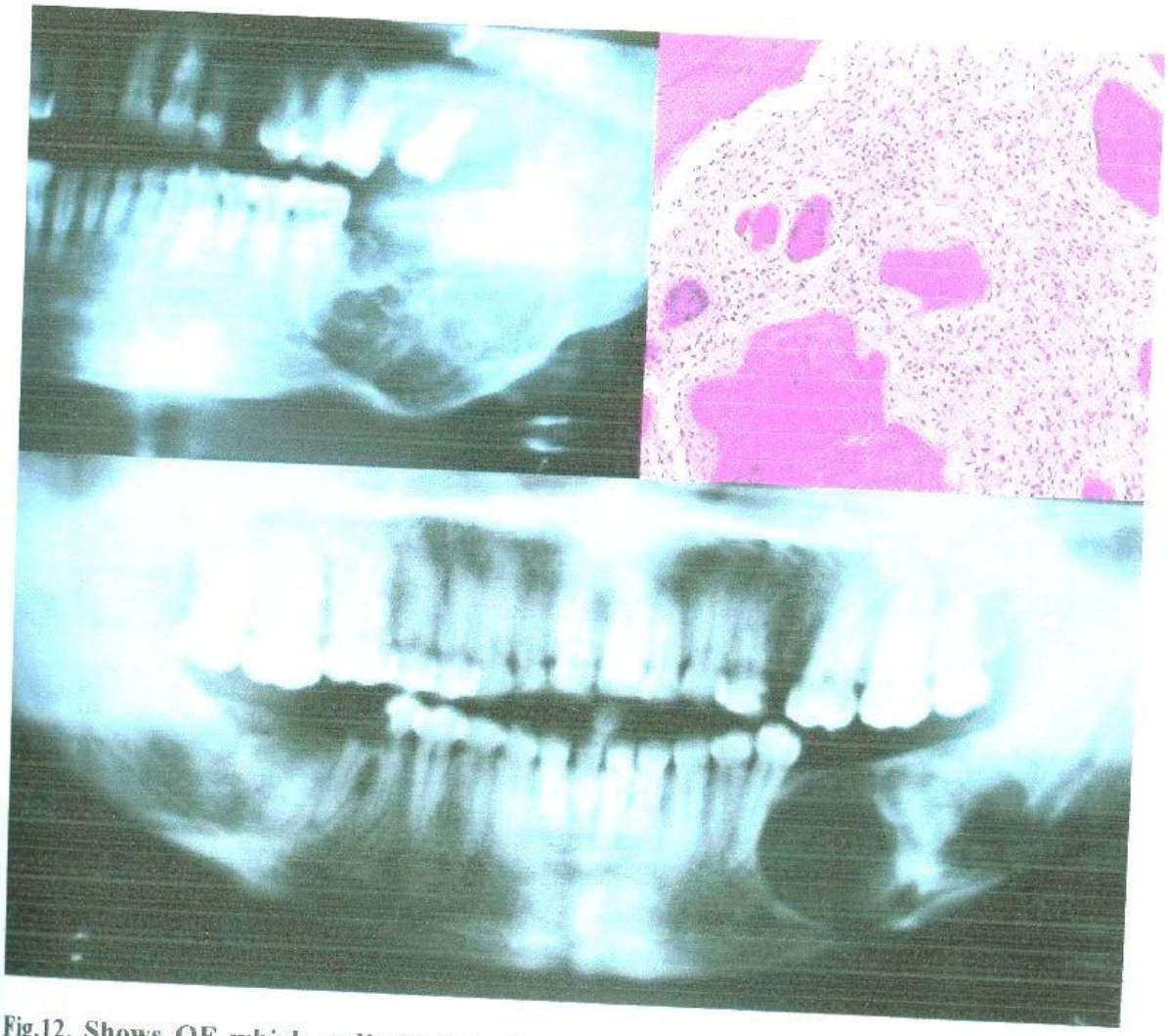


Fig.12. Shows OF which radiographically presents a mixed type pattern of well-defined borders with sclerotic margins; and the inset depicting its typical histopathologic features (Original magnification x 200, H&E)

## 4.0 DICUSSION

The present study has shown that although some histopathologic and radiographic features can separate FD from OF, it is still difficult to arrive at a definitive diagnosis by using a single diagnostic modality. According to the WHO classification of odontogenic tumours[22, 63], OF and COF are defined as similar lesions since they are demarcated or encapsulated neoplasms consisting of fibrous tissue containing varying amounts of mineralized material ( bone and / or cementum) . In the present study there were more females than males affected by both lesions. Although a higher proportion of females were affected by OF compared to males, the difference was not statistically significant. These results correlate with other studies[2, 35, 57, 62] that females are more affected than males. This observation may be due to the fact that female sex hormones or hormonal changes could be responsible for triggering the growth of these lesions.

The occurrence of these lesions in the 1st to 6th decades of life reflects their early development, slow growing nature as well as their asymptomatic nature. This indicates that, early detection by routine screening of the population and their early treatment could reduce their occurrence and subsequent deformation of the affected people. The study also demonstrated that as age increased there was a decrease in the occurrence of these lesions. The observation may imply that aging may not play a part in the development of these lesions. In the present study the mandible was more affected by these lesions compared to the maxilla. OF tended to occur more in the mandible compared to the maxilla while FD tended to occur more in the maxilla compared to the mandible. However, the reason for this distribution is not known although it has been proposed that inflammatory processes secondary to either infections or trauma may cause the development of these lesions. It is conceivable that different populations of cells may respond in a lineage-dependent manner to mechanical stress in terms of their amount of CAMP and insulin-like growth factor-I and hence could be the reason for this distribution .In addition, the anatomic and functional heterogeneity within individual bone units could be the reason for this distribution.

Analysis of the 72-cases which had specific sides recorded (left or right) showed that the left side of the maxilla was the most affected by both lesions. Although there was the tendency of the left maxilla to be more affected, these results differ from previous studies in the literature

[4,16]where it was noted that FD had a predilection for the right side of the maxilla. This difference might be attributed to differences in methodology and number of cases evaluated in these studies. Thirty eight radiographs of OF and FD were available for evaluation among which OF comprised 26 radiographs while 12 were those of FD. OF showed five radiographic appearances while FD showed three. Several studies have reported different radiographic patterns for OF and FD. Ye et al.[19]reported three radiographic patterns for FD namely sclerotic, osteolytic and mixed type. Lu et al.[34] reported four radiographic patterns for OF namely cystic radiolucency, ground glass appearance, sclerotic change and the mixed type while Barberi et al. [59]reported three radiographic patterns for COF namely radiolucent (53 %), sclerotic (7 %) and mixed type (40 %).

In all these reports including the present one, there is overlapping of the radiographic appearances of OF and FD. This overlapping of radiographic patterns between FD and OF implies that these lesions are not static and so they keep on changing as maturation occurs within them. The Radiographic correlations are valuable in the differential diagnosis of FD and OF, although some similarities may be encountered in both entities. Statistical analysis in the present study has revealed several features specific for each lesion. Most OF display predominantly opacity, radiolucency or mixed lucency /opacity with well defined margins with or without sclerotic borders. The findings correlate well with the progress of the lesion as it appears histopathologically. Because of its progressive mineralization, the radiographic appearance depends on the stage of development. An ill-defined radiolucency which was most frequently seen in the early stage should be differentiated from FD. A well defined radiolucency with or without sclerotic borders is typically seen in OF. This radiographic appearance is often associated with jaw expansion and these lesions may occasionally have ill-defined borders if relative growth occurs. Histopathologically, this type of OF shows scanty bony trabeculae with a predominance of cellularity. A mixture of radiolucency and opacity is the most common appearance of OF and always has a well-defined border with a variable degree of jaw expansion. A fibrous capsule or an attenuated layer of cortical bone may be present microscopically.

A pure radiodensity (a homogenous opacity with a very smooth outline) is also found in OF. It may mimic the appearance of osteoma or complex odontoma and usually does not cause jaw expansion .It should be emphasized that, radiographic distinction of OF and FD has its limits, especially for small OF lesions and unusually large FD lesions. Therefore, adequate biopsy with correlation of histopathologic features is essential to reach an accurate diagnosis. Also radiographic features alone should not be relied upon to execute surgical procedures since this

may result in either under- treatment or over- treatment. The diverse number of conditions which resemble these lesions radiographically may include chondromas, chondrosarcoma, osteoid tumours, osteosarcoma, Pagets' disease of bone, chronic osteomyelitis and cemento-osseous dysplasia. These conditions produce a matrix, the intracellular substance that can calcify or ossify and resemble OF and FD radiographically. Radiographic appearance will only give you a clue as to the differential diagnosis of these lesions and they need to be confirmed by other diagnostic modalities such as the clinical history and histopathology.

The absence of the radiolucent and radiopaque pattern for FD could be explained by the fact that radiographic appearance of this lesion varies according to the degree of maturation which determines the degree of opacification. The initial radiographic pattern of FD is radiolucent and the radiolucent pattern also occurs in a number of conditions such as giant cell granuloma, traumatic bone cyst, aneurysmal bone cyst and cemento-ossifying fibroma. Therefore, the early lesion of FD with a radiolucent pattern could have been misdiagnosed as giant cell granuloma, aneurismal bone cyst, traumatic bone cyst or cemento-ossifying fibroma .On the other hand, the radiographic appearance depends upon the amount of fibrous tissue that replaces bone and its distribution. Radiopacities occur when these fibrous elements have undergone calcification.

Evaluation of the borders showed that OF presents with well defined borders with or without sclerotic margins and ill-defined margins. .FD presents with well defined borders without sclerotic margins and ill-defined margins. The results of this study parallel previous studies in the literature [2,15,34,60] .The degree of definition of the margins of FD is a very important diagnostic feature that allows the ready definition of FD from the OF. Regardless of the stage of maturation, an important diagnostic feature of OF is the well-defined borders when compared to FD. A well-defined radiolucency with or without sclerotic borders is typically seen in OF and these lesions may occasionally have ill-defined borders if there is a relatively rapid growth.

A well-defined, sharply marginated lesion indicates slower growth than ill-defined non-marginated lesion. This means that FD has a higher growth rate when compared to OF. However, radiographs have limitation in the diagnosis of these lesions. Radiographs can differentiate FD from OF since FD has ill-defined margins while the latter has well–defined margins. Furthermore, it is difficult to differentiate OF from FD radiologically during the initial stage of development. Notably, the loss of lamina dura could be used as an ancillary diagnostic feature for FD[60]

The pathologic distinction of FD and OF on a histopathological basis alone have been quite difficult, if not impossible, because of the extensive overlap between histopathologic features that characterized the two lesions[7, 20, 22]. Microscopic similarities illustrate this point since both lesions have separate bony trabeculae, variable amounts of lamella bone with a storiform pattern, dense and loose collagen .Metaplastic woven bone in a fibrous stroma was equally observed in FD and OF. it is, therefore, not surprising that the majority of FDs in the present study were diagnosed as OF. Although there were similarities in pathological parameters in both lesions, differences were found between the two lesions. The significance of these observations is illustrated by a statistical analysis indicating that FD is different from OF not only in clinical and radiographic presentation but also in histopathology. Distinguishing FD from OF is essential since the surgical treatment of the two lesions is different .For example almost all cases of FD in this study were treated by curettage. In contrast OF were treated by enucleation or block resection. FDs are tumours with ill-defined borders and their margins between the normal and affected part of bone usually poorly defined .At surgery they tend to be removed with difficulty.

A reliable distinction of FD and OF microscopically could have depended on the combination of several specific pathologic features rather than a single morphologic criterion. In the present study , the pathological features including osteoblastic rimming, giant cells and the presence of a capsule had been shown to be a possible pathological parameter in distinguishing FD from OF. However, a large study is recommended to establish whether these histopathological parameters can distinguish OF from FD reliably. No single histopathologic feature could render a definitive diagnosis for either FD or OF no matter how characteristic it might seem. According to Boysen et al.[61] both FD and OF present the same histomorphological features but they vary by the presence of spheroidal calcifications found only in OF. This has been demonstrated in this study. The findings illustrate an important fact that although pathologic features can be used to separate FD and OF, clinical and radiographic information is important for accurate diagnosis.

## 4.1 conclusion

In this study it was not possible to separate OF from FD by radiologic or histopathologic features since there was overlapping of these features between the two lesions.

## 4.2 Recommendations

1. The results of this study have demonstrated some histopathological features which can be used to separate OF and FD. Therefore, there is a need of conducting large study (multicentre approach) on these lesions in order to develop clear clinical histopathologic criteria for differentiating FD and OF.
2. Special stain studies, for example the Vonkossa technique which was tested on a few paraffin embedded tissues of FD and OF; and has shown the ability to demonstrate calcium in these lesions. Special stain studies and Immunohistochemical studies using monoclonal antibodies are important studies which may help in providing an insight into the nature of the matrix and mineralized tissues of these lesions.
3. Proper record keeping is important for successful research outcomes.

## 4.3 Study limitations

1. Records section: The records section was not organized. Some files and x- rays were missing. Sometimes the files missed important information needed for this study.
2. Laboratory: The University laboratory is well equipped with talented staff. However, the following areas are wanting:

    I. Important pieces of equipment for performing a study like this were either absent or out of order.

    II. As a result the range of histochemical tests performed on decalcified, paraffin embedded tissue was limited by lack of material and equipment so that tests such as Gomori's silver impregnation, Elastica Van Gieson, Vonkossa and Periodic acid Schiff which were required to elucidate the nature of the matrix and mineralized tissues in this study were not carried out.

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