OSSIFYING FIBROMA: A CLINICAL AND
RADIOLOGICAL STUDY AT THE
UNIVERSITY OF THE WESTERN CAPE
ORAL HEALTH CENTRE

A thesis submitted in fulfillment of the requirements for the degree of
Magister Scientiae Dentium in the Department of Maxillo-Facial and Oral
Surgery, Faculty of Dentistry, University of the Western Cape

Supervisor: Prof. J.A. Morkel

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Ossifying Fibroma: a clinical and radiological study at the University of the Western Cape Oral Health Centre

Fadi Titinchi

KEYWORDS

Ossifying fibroma
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Fibro-osseous lesions
Juvenile ossifying fibroma
Cementifying fibroma
Synchronous ossifying fibroma
Aneurysmal bone cyst
Fibrous dysplasia
Pantomograph
Mandible
Maxilla
ABSTRACT

Ossifying Fibroma: a clinical and radiological study at the University of the Western Cape Oral Health Centre

Fadi Titinchi

MSc (Dent) thesis, Department of Maxillo-Facial and Oral Surgery, Faculty of Dentistry, University of the Western Cape.

Ossifying fibroma (OF) is the most frequent of the three fibro-osseous lesions of the jaws. It occurs mostly in patients between the age of 20 and 40 years. Females are more commonly affected than males. Clinically, OF usually presents as a painless expansive intra-bony mass. Swelling and pain may be present in some cases while some lesions are discovered incidentally. Radiographically, OF is usually well-defined and unilocular or multilocular. Early lesions present as well-defined radiolucency that are small in size. Over time, the lesions tend to enlarge in size and become mixed radiolucent-radiopaque and finally become completely radiopaque.

The aim of this study was to determine the clinical and radiological features of ossifying fibroma presenting at the Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology, University of the Western Cape Oral Health Centre as well as to assess its management and recurrence patterns.

A retrospective case series analysis was performed of all histopathologically diagnosed ossifying fibroma cases available at the Departments of Maxillo-Facial and Oral
Surgery and Diagnostics and Radiology at the Faculty of Dentistry, University of the Western Cape from 1976-2014.

Patient’s age, gender and ethnicity were recorded. The clinical presentation of the lesion as well as the history was analyzed. Radiographic features including density, size, shape, location, locularity and its effect on adjacent structures was noted. Management of each case and follow-up was also documented.

A total 61 cases were included in the study. The majority of patients were females (63.9%) and below 40 years of age (73.9%). Few cases were symptomatic (29.5%) with an average period 22 months from first symptoms to presentation. The mandibular posterior region was most affected (55.5%) while larger lesions occurred more frequently in younger patients. Majority of lesions were radiopaque (49.2%) and had well-defined margins (93.6%). Most cases were managed by surgical curettage (68.2%). Following an average follow-up period of 20 months only one case recurred (recurrence rate =6.7%).

In conclusion, the majority of the clinical and radiographic findings of ossifying fibroma were similar in South African patients as those of other populations. Differences include that the lesions in this population were more radio-opaque and larger in size than in the reported literature. Surgical curettage is an acceptable management protocol with low rate of recurrence.

March 2016
DECLARATION

I declare that *Ossifying Fibroma: a clinical and radiological study at the University of the Western Cape Oral Health Centre* is my own work, that it has not been submitted for any degree or examination in any other university, and that all sources I have used or quoted have been indicated and acknowledged by complete references.

Fadi Titinchi

March 2016

Signed...................................................
ACKNOWLEDGEMENTS

This research project could not have been accomplished without the guidance and support of the following individuals:

- I would like to express my sincere gratitude to my study supervisor Prof. Jean Morkel (Academic Head of Department of Maxillo-Facial and Oral Surgery) for all his support and valuable input throughout the study. His continuous encouragement and guidance has been very valuable for the completion of this study.
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- My parents and family for their constant assistance and moral support throughout the years of my studies.
DEDICATION

This thesis is dedicated to my beloved parents for all their love and support throughout the years.
CONFERENCES AND PUBLICATIONS

The work in this dissertation was presented at the following conference:


The following articles were published during the period of study:


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GLOSSARY

The following terms below will be clarified for the purpose of this study:

- **Cortication**: describes the presence of radio-opaque rim around the margins of the lesion. It typically characterizes the body’s response to the tumour by deposition of new bone at the periphery of the lesion resulting in radio-opaque margin.

- **Curettage**: describes a surgical procedure in which a curette is used to remove diseased tissue by scooping or scraping.

- **Enucleation**: describes a surgical technique in which the entire tumour or lesion is removed without the need for any dissection.

- **Expansion**: describes the ability of the lesion to expand and increase in size within the bone.

- **Infiltration**: describes the ability of a lesion to invade and infiltrate the surrounding tissue.

- **Loculation**: describes the appearance of a lesion on a radiograph which is formed of multiple compartments within the bone (multilocular) or a single compartment (unilocular).

- **Margin of the lesion**: describes the border or interface between the lesion and the normal surrounding tissue.

- **Opacification**: describes a pathologic change in a lesion which leads to a radio-opaque presentation on radiograph.

- **Resection**: describes a surgical procedure whereby a diseased body part is removed completely or partially.
• **Septae**: describes a term used to define bony walls within a lesion. These walls can be coarse or fine and in certain lesions separate the tumour into numerous compartments.

• **Well-defined lesion**: describes a lesion with a zone of transition of less than 1 mm from the normal surrounding bone.
Chapter 1

INTRODUCTION

The maxillofacial and oral region is an anatomical site consisting of the jaws (maxilla and mandible), oral cavity and related soft tissues. Numerous neoplastic conditions and lesions can occur in this region with variable levels of destruction. Tumours occurring in the jaws, and especially the mandible, occur more frequently than lesions arising in the mid facial region (Riaz and Warriach 2011). Tumours of the jaws are generally classified as either of odontogenic or non-odontogenic in origin. These tumours can also be further classified into benign and malignant lesions.

Fibro-osseous lesions are a poorly defined group of non-odontogenic tumours affecting the jaws and craniofacial bones. This term is not a definite diagnosis but only hints at a general group of several lesions (Gondivkar et al. 2011). The three main categories of fibro-osseous lesions according to the World Health Organisation (WHO) classification include fibrous dysplasia, ossifying fibroma, and osseous dysplasia (Akcam et al. 2012) (Table 1).
Table 1: World Health Organization classification of fibro-osseous lesions of the jaws (2005).

1. Fibrous dysplasia

   - Monostotic fibrous dysplasia
   - Polyostotic fibrous dysplasia

2. Osseous dysplasia

   - Periapical osseous dysplasia
   - Focal osseous dysplasia
   - Florid osseous dysplasia

3. Ossifying fibroma

   - Juvenile trabecular ossifying fibroma
   - Juvenile psammomatoid ossifying fibroma

In all lesions in this group, the normal bone structure is replaced by fibroblasts and collagen fibres consisting of variable amounts of mineralized material. They are uncommon benign tumours that show many similarities clinically, radiographically and histopathologically. Diagnosis of fibro-osseous lesions based on histopathological features alone has substantial limitations (Waldron 1985). Hence accurate classification of these lesions necessitates correlation of the history, clinical presentation, radiographic features, operative findings, and histological appearance (Gondivkar et al. 2011).
Chapter 2

LITERATURE REVIEW

A variant of ossifying fibroma (OF) was first described in 1872 by Menzel in a 35 year old female presenting with a large tumour of the mandible (Gondivkar et al. 2011). In 1927, Montgomery was the first author to coin the term ossifying fibroma, by which the lesion is currently known. Prior to 1948, it was thought that fibrous dysplasia and OF were variants of same lesion. Sherman and Sternberg (1948) were the first authors to presented a detailed report on the clinical, radiological and histological features of OF, and subsequently most researchers concur that the fibrous dysplasia and OF are two different clinical entities (Gondivkar et al. 2011).

In 1968, Hamner et al. grouped all cementum-containing tumours into one category known as fibro-osseous lesions; however, the term “Ossifying Fibroma” has been in use since 1927. This lesion has been known by numerous names including non-osteogenic fibroma, cemento-ossifying fibroma, osteofibrous dysplasia, osteofibroma and fibro-osteoma. It was previously also identified as osteofibrous dysplasia which was first reported by Campanacci (1976), where the lesion presented in the fibula and tibia. Jaffe and Lichtenstein (1942) described the same lesion above as nonosteogenic fibroma, also commonly known as “Jaffe-Campanacci syndrome”.

The World Health Organization (WHO) in 1971 classified four main types of cementum-containing lesions which included: fibrous dysplasia, ossifying fibroma,
cementifying fibroma and cemento-ossifying fibroma (Pindborg and Kramer, 1971). In the second WHO classification in 1992, benign fibro-osseous lesions in the Maxillo-facial region were separated into two groups, osteogenic neoplasm and non-neoplastic bone lesions. Cementifying ossifying fibroma belonged to the osteogenic group of neoplasms (Kramer et al. 1992). In the latest WHO classification of 2005, the term “Cementifying Ossifying Fibroma” was replaced with “Ossifying Fibroma” (Reichart et al. 2006). Brannon and Fowler in 2001 appear to have started the trend to use ossifying fibroma instead of cementifying ossifying fibroma and this was continued by Reichart et al. (2006) and numerous other authors in the literature.

2.1. Aetiology

Ossifying fibroma is an osteogenic tumour with membranous ossification. It hence involves solely the maxillofacial bones (Trijolet et al. 2011). It is thought to originate from the periodontal ligament which contains multi-potential cells capable of forming fibrous tissues, cementum and lamellar bone. This thought is supported by the fact that some lesions contain cementum-like calcifications while others only contain bony material; however, a mixture of the two types of calcifications is frequently present in a single lesion (Liu et al. 2010; Kramer et al. 1992).

For a number of years, it has been advocated that the origin of OF is odontogenic arising mainly from the periodontal ligament (Kramer et al. 1992). However, recent presentation of microscopically indistinguishable lesions in the frontal, temporal, sphenoid and ethmoid bones made this assumption disputable. There are two probable explanations for manifestation of ossifying fibromas outside the jaws. Firstly, the lesion
can develop from ectopic periodontal membrane, and the second explanation is that the periodontal membrane is a mesodermal germ layer. Some primitive mesenchymal cells are capable of differentiating in a similar manner to produce a tumour (Trijolet et al. 2011).

The pathogenesis of OF remains unknown: it is thought to be associated with congenital complications in maturation of dental tissue, which is capable of forming both cement and bone (Trijolet et al. 2011). According to Marx and Stern (2002), OF arises commonly in the jaws as these lesions are linked to an extensive mesenchymal cellular induction into bone and cementum, required in odontogenesis. Hence, when an error in the tissue induction process occurs, an OF can develop in the jaws as a result. Some authors have also suggested that trauma in the area of the lesion, such as the extraction of dentition or the preceding presence of periodontitis, are likely to be trigger factors for the development of the lesion (Martín-Granizo et al. 2000).

### 2.2. Epidemiology

Ossifying fibroma is considered by some authors as the most common benign fibro-osseous lesion of maxillofacial and oral region (Ogunsalu et al. 2001). It occurs mostly in patients between the ages of 20 and 40 years, although it may present in children and adolescents as well as in older adults. Hence patients of any age may be affected. Females are more commonly affected than males with a ratio of 5:1 (Akcam et al. 2012).

Ossifying fibroma has been described in almost every racial group and has also been reported in numerous population groups (Table 2). It does not show any predilection for
any particular racial group or population. Very little is known about the prevalence of this lesion in sub-Saharan Africa due to the lack of reports in the literature. As shown in Table 2, the majority of reports have been conducted in North American and East Asian communities (MacDonald-Jankowski 2009). Most patients in these samples are Caucasian and ethnic Chinese in origin respectively. Few reports were conducted in Indian, Brazilian and Hispanic populations.
Table 2: List of all population based studies (five or more cases) on ossifying fibroma reported in the literature.

<table>
<thead>
<tr>
<th>Author</th>
<th>Population group</th>
<th>No. of patients</th>
<th>Time period (no. of years)</th>
<th>Ethnicity</th>
<th>Male: Female ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mohanty et al. (2014)</td>
<td>Indian</td>
<td>25</td>
<td>2001-2011 (10 years)</td>
<td>I: 25 (100%)</td>
<td>14:11</td>
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<tr>
<td>Ojo et al. (2014)</td>
<td>South African</td>
<td>56</td>
<td>NA</td>
<td>B: 47 (83.9%) W: 9 (12.5%)</td>
<td>17:39</td>
</tr>
<tr>
<td>de Andrade et al. (2013)</td>
<td>Brazilian</td>
<td>8</td>
<td>2000-2010 (10 years)</td>
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</tr>
<tr>
<td>Triantafillidou et al. (2012)</td>
<td>Greek</td>
<td>14</td>
<td>NA</td>
<td>NA</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Sopta et al. (2011)</td>
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<td>10</td>
<td>1991-2005 (15 years)</td>
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</tr>
<tr>
<td>MacDonald-Jankowski and Li (2009)</td>
<td>Hong Kong</td>
<td>24</td>
<td>1982-2004 (22 years)</td>
<td>C: 24 (100%)</td>
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</tr>
<tr>
<td>Chang et al. (2008)</td>
<td>Taiwanese</td>
<td>28</td>
<td>1988-2006 (18 years)</td>
<td>C: 28 (100%)</td>
<td>6:22</td>
</tr>
<tr>
<td>Olgac et al. (2006)</td>
<td>Turkish</td>
<td>39</td>
<td>1971-2003 (33 years)</td>
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<tr>
<td>Jones et al. (2006)</td>
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<td>33</td>
<td>1973-2002 (30 years)</td>
<td>INA</td>
<td>8:25</td>
</tr>
<tr>
<td>Simon et al. (2002)</td>
<td>Tanzanian</td>
<td>30</td>
<td>1982-1997 (15 years)</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>Study</td>
<td>Region</td>
<td>Cases</td>
<td>Years</td>
<td>Subgroup</td>
<td>Event</td>
</tr>
<tr>
<td>------------------------------------</td>
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<td>Albuquerque et al. (2000)</td>
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<td>26</td>
<td>1970-1997 (28 years)</td>
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<td>Polish</td>
<td>11</td>
<td>1956-1996 (41 years)</td>
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<tr>
<td>Su et al. (1997)</td>
<td>American</td>
<td>75</td>
<td>INA</td>
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<td></td>
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<tr>
<td>Mosqueda-Taylor et al. (1997)</td>
<td>Mexican</td>
<td>5</td>
<td>1960-1996 (37 years)</td>
<td></td>
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</tr>
<tr>
<td>Summerlin and Tomich (1994)</td>
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<td>45</td>
<td>INA</td>
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<td>B: 10 (22.2%)</td>
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<tr>
<td>Swaroop et al. (1990)</td>
<td>Indian</td>
<td>8</td>
<td>1963-1981 (19 years)</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Slootweg and Muller (1990)</td>
<td>Dutch</td>
<td>12</td>
<td>INA</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Zhou (1989)</td>
<td>Chinese</td>
<td>29</td>
<td>1966-1985 (20 years)</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Yoon et al. (1989)</td>
<td>South Korean</td>
<td>16</td>
<td>1977- 1986 (10 years)</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Van Heerden et al. (1989)</td>
<td>South African</td>
<td>30</td>
<td>INA (6 years)</td>
<td>INA (majority black)</td>
<td>IN</td>
</tr>
<tr>
<td>Agrestini et al. (1987)</td>
<td>Italian</td>
<td>6</td>
<td>INA</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Rados (1986)</td>
<td>Chilean</td>
<td>12</td>
<td>INA</td>
<td></td>
<td>INA</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Duration</td>
<td>Year Range</td>
<td>Race Distribution</td>
<td>White: Black: Chinese: Hispanic: Indian: Information Not Available</td>
</tr>
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<td>-------------------</td>
<td>----------------</td>
<td>-------------</td>
<td>-------------------</td>
<td>---------------------------------------------------------------</td>
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<tr>
<td>Wu and Chan (1985)</td>
<td>Hong Kong</td>
<td>11</td>
<td>1963-1982</td>
<td>INA</td>
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<tr>
<td>Eversole et al. (1985)</td>
<td>American</td>
<td>64</td>
<td>INA</td>
<td>W: 50% B: 16% C: 10% H: 21%</td>
<td>12:52</td>
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<tr>
<td>Adekeye et al. (1980)</td>
<td>Nigerian</td>
<td>7</td>
<td>INA</td>
<td>INA</td>
<td>3:4</td>
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<tr>
<td>Sakota (1977)</td>
<td>Japanese</td>
<td>28</td>
<td>INA</td>
<td>INA</td>
<td>9:19</td>
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<tr>
<td>Langdon et al. (1976)</td>
<td>British</td>
<td>10</td>
<td>1966-1975</td>
<td>W: 9 (90%) B: 1 (10%)</td>
<td>3:7</td>
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<td>Kawai et al. (1974)</td>
<td>Japanese</td>
<td>18</td>
<td>INA</td>
<td>INA</td>
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<td>Waldron and Giantsanti (1973)</td>
<td>American</td>
<td>43</td>
<td>1957-1971</td>
<td>B: 21 (48.8%) W: 12 (27.9%)</td>
<td>7:36</td>
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<td>Schmaman et al. (1970)</td>
<td>South African</td>
<td>23</td>
<td>INA</td>
<td>B: 23 (100%)</td>
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<td>Nigerian</td>
<td>19</td>
<td>INA</td>
<td>INA</td>
<td>6:12 (1 unknown)</td>
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</table>

W: White; B: Black; C: Chinese; H: Hispanic; I: Indian; INA: Information Not Available.
2.3. Clinical presentation

Clinically, OF usually presents as a painless spherical or ovoid expansive intra-bony mass. Patients usually present with a symptomless slow growth. However, in certain cases, pain or paraesthesia may be present if the adjacent nerve is affected. OF can also cause sinus obstruction, facial deformity, proptosis and intracranial complications, even though it can stay asymptomatic during the early stages of development (Gondivkar et al. 2011).

Large OF can present with expansion of the buccal and lingual plates while cortical erosion is rare. Larger lesions are able to expand the lower border of the mandible. This expansion of the affected bone may lead to noticeable disfigurement and ulceration of the oral mucosa from occlusion by the opposing dentition. The overlying oral epithelium typically remains intact unless secondarily infected (Akcam et al. 2012).

In some cases, the lesion can develop into a massive size and may cause significant cosmetic and functional deformity (Khanna and Andrade 1992). It has the ability to displace dentition without affecting the vitality of those adjacent teeth and do not show any signs of necrosis. The lesion is generally firm in consistency, subject to the degree of mineralization within the lesion. Intra-orally, the lesions are covered with normal mucosa and there are no signs of associated adenopathies (Trijolet et al. 2011).

2.4. Location

The mandible is the most affected bone (75%) compared to the maxilla. The mandibular molar and premolar regions are the most affected followed by the maxillary anterior region (Triantafillidou et al. 2012; Sopta et al. 2011). The lesion can also occur in other
cranial and facial bones including frontal, ethmoid, sphenoid, and temporal bones as well as the paranasal sinuses. It rarely involves the long bones (Gondivkar et al. 2011).

2.5. Radiographic features

Ossifying Fibromas are usually well demarcated and occasionally corticated. It usually presents as either a cystic lesion (unicystic or multicystic) or as mixed-density lesion (Akcam et al. 2012). The radiographic features of OF depends on the duration of the lesion present. Early lesions present as well-defined radiolucency that is small in size and has ground glass appearance (Sopta et al. 2011). Over time, the lesions tend to enlarge in size and become mixed radiolucent-radiopaque with opacities appearing in the middle of the lesion that are of lower density than the surrounding bone. When lesions mature, they appear with asymmetrical opacities forming concentric bony trabeculae, surrounded by peripheral osteo-condensation, often described as an eggshell appearance (Trijolet et al. 2011). Lesions are seldom predominantly opaque and these features help distinguish OF from fibrous dysplasia (Akcam et al. 2012; MacDonald-Jankowski 1998).

The borders of the lesions appear fairly smooth with a regular contour. The lesion appears to be concentric inside the medullary part of the bone with outer expansion nearly equal in all directions. This can lead to expansion of the outer cortical plate of the affect jaw bone. Despite this expansion and thinning of the outer cortical bone, the lesion does remain intact without breach of the cortex. The expansion of the tumour, however, can cause displacement of the adjacent dentition or the inferior alveolar canal and maxillary antrum. The lamina dura of affected adjacent dentition is frequently
missing and the roots of these affected dentition may show signs of resorption (Liu et al. 2010; MacDonald-Jankowski, 2004).

Ossifying fibroma usually presents with well-defined margins in the jaws. It has been described that lesions with a transition zone of less than 1 mm can be described as well-defined. This feature can be easily identified by conventional radiographs and was described by the first edition of the WHO classification as the distinguishing feature between fibrous dysplasia and OF; the former lesion presenting with a poorly-defined margin, while the latter presenting with a well-defined margin (MacDonald-Jankowski and Li, 2009).

Ossifying fibroma is usually slow-growing in nature but can behave quite aggressively leading to local destruction of bone and adjacent structures. Some of these aggressive expansile lesions can involve the entire jaw bone. On radiographs, these lesions often show medium-density mass with cancellate dense lines in it known as septae (Liu et al. 2010). Expansive mandibular lesions may also cause a characteristic thinning and downward “bowing” of the inferior border of the mandible (Triantafillidou et al. 2012).

To differentiate ossifying fibroma from fibrous dysplasia on radiographs, it is important to identify the site, growth pattern and borders of the lesion. Fibrous dysplasia occurs more frequently in the maxilla and tends to grow longitudinally, in comparison to the compressed spherical growth of OF. Also, the radiographic borders of OFs are well-defined as compared to fibrous dysplasia which is usually poorly defined (Akcam et al. 2012).

Computed tomography (CT) and magnetic resonance (MR) imaging play a vital role in assisting the clinician to arrive at an accurate diagnosis and to determine the extent of
the lesion (Khoury et al. 2002). However, the number of reports on CT and MR findings in the literature is limited due to high costs involved and limited access to these advanced imaging modalities in many countries.

Ossifying fibroma usually appears as expansile on CT scans with well-demarcated borders and thin sclerotic margins. It shows signs of a locally aggressive neoplasm with cortical interruption and involvement of adjacent anatomical sites. The lesion content consists of mainly soft tissue with variable amount of internal bony calcifications appearing as linear or irregular. Some lesions displace regions of low CT density which is usually indicative of cystic changes within the lesion. In some cases, the patient is intravenously injected with iodinated contrast medium to show diffuse enhancement. On CT scan the differential diagnosis list should include fibrous dysplasia and cemento-osseous dysplasia (Mithra et al. 2012).

To differentiate ossifying fibroma from fibrous dysplasia on CT scans, fibrous dysplasia usually has ground glass appearance, expands the involved bone longitudinally and shows ill-defined borders. The three variants of cemento-osseous dysplasia are localized lesions usually arising entirely in the tooth-bearing regions of the jaws; however, larger lesions may be difficult to differentiate from ossifying fibroma (Mithra et al. 2012).

Magnetic resonance imaging plays a crucial role in evaluating the extent of the lesion however it is of no value in defining the bony component of the lesion. On T1-weighted images, the lesion is isointense to muscles and on T2-weighted images hypo- or isointense to muscles. Areas of cystic formation may be present. The lesion shows low to intermediate signal intensity on spin-echo sequences and following administration of gadolinium contrast, there is some degree of homogeneous lesion enhancement (Khoury et al. 2002).
2.6. Microscopic features

Ossifying fibroma presenting in the jaws can only be diagnosed histologically as a fibro-osseous lesion and cannot be confirm as OF on histological basis alone (Waldron, 1993). Fibro-osseous lesions are a histopathological group of lesions including fibrous dysplasia, florid osseous dysplasia and focal osseous dysplasia. Waldron (1993) stated that the lack of sound clinical and radiographic information can only allow the pathologist or clinician to diagnose a specimen as a fibro-osseous lesion. However, with sufficient clinical and radiographic information, most lesions can be diagnosed with fair certainty into one of the subcategories of fibro-osseous lesions.

The histological features of OF are typical and help to differentiate it from the other fibro-osseous lesions of the jaws (Sopta et al. 2011). The typical histopathology of OF is an encapsulated lesion consisting of stroma which is highly-cellular with the majority of cells being fibroblasts. The majority of OF contain both bone and cementum-like elements which gives this lesion a histological appearance ranging from bone to cementum. Such an image hints that these two components most likely arose from the same progenitor cell (MacDonald-Jankowski 1998).

Ossifying fibroma is composed of two main components: fibrous stroma and bone elements that display several degrees of maturation. The fibrous stroma contains proliferating fibroblasts and collagenous fibres. Bone elements comprise of ossicles, osteoids, woven bone and lamellar bone (Sopta et al. 2011).

Ossicles are mineralized bodies that join to form bone trabeculae that are typically surrounded by osteoblasts and infrequently by osteoclasts. Circular cementum-like bodies are occasionally present either alone or along with trabeculae. Due to the
deviation in the outline of these calcified deposits, such lesions have been described to as both ossifying and cementifying fibroma (Sopta et al. 2011).

2.7. Diagnosis

Distinguishing between OF and other fibro-osseous lesions is sometimes difficult due to the similarity in clinical, radiographic and histologic features (Vegas-Bustamante et al. 2008). Identifying between fibrous dysplasia and OF is the primary differential diagnostic challenge. The most important distinguishing factor between fibrous dysplasia and OF is that OF has a well demarcated appearance on radiographs while fibrous dysplasia is poorly differentiated with ground glass appearance. OF can also be separated with ease from normal bone during surgery while fibrous dysplasia cannot be easily identified from healthy bone (Trijolet et al. 2011).

Histologically, these two lesions are difficult to differentiate during early stages. Fibrous dysplasia is described to contain woven bone only, without the presence of osteoblastic rimming of bone. The finding of mature lamellar bone histologically is characteristically indicative of OF (Marx and Stern 2002; Triantafillidou et al. 2012).

Ossifying fibroma may also resemble a cementoblastoma or florid cemento-osseous dysplasia when it occurs around the roots of teeth. OF can be distinguished from these rare lesions by their differing radiographic features. The cementoblastoma is fused to the root of the affected tooth, and florid cemento-osseous dysplasia displays several sclerotic densities in the alveolar bone involving one or both jaws (Marx and Stern 2002; Triantafillidou et al. 2012).
2.8. Management

The most common method of managing OF is surgical excision. Small and well defined lesions can be excised by enucleation and curettage, whereas, large expanding lesions require radical surgery within healthy margins and aesthetic recontouring (Triantafillidou et al. 2012). The decision on whether to enucleate or resect radically, depends on a number of factors including involvement of the lower border of the mandible and expansion of the lesion in the adjacent soft tissues or the maxillary sinus and nasal cavity (Vegas-Bustamante et al. 2008; Marx and Stern 2002). Both these surgical approaches to treatment of OFs are reported to be acceptable by most authors in the literature during the past 30 years (Triantafillidou et al. 2012).

Chang et al. (2008) reported that the most common clinical sign of OF was swelling and expansion of the buccal and/or lingual cortical plates. The preferred treatment of OF was surgical resection. However, Sciubba and Younai (1989) recommended that curettage or enucleation of the tumour should be the first line of treatment.

Radiotherapy in the management of patients with ossifying fibroma is contra-indicated due to the radio resistant nature of the lesion and post radiation complications (Jung et al. 1999). Radiotherapy has also been shown to increase malignant transformation rate of the lesion from 0.4% to 40% with the exception of certain subtypes of ossifying fibro-myxoid tumour. (Baumann et al. 2005).

Chemotherapeutic agents described in the literature in the management of ossifying fibroma include used of interferon alpha and subcutaneous calcitonin therapies. Kaban et al. (2002) have advocated the use of subcutaneous interferon alpha for one year following enucleation or curettage when managing cases of aggressive juvenile
ossifying fibroma in the maxilla, paranasal sinuses or orbit. This form of therapy has been shown to be effective in the management of giant cell lesions following curettage or enucleation due to its anti-angiogenic effect (Abuzinada and Alyamani, 2010).

Subcutaneous calcitonin therapy, which is an inhibitor of osteoclastogenesis and proliferation, has been described to be effective in the management of central giant cell granuloma. A randomized double-blind controlled study by de Lange et al. (2006) included 14 patients with central giant cell granuloma of the jaw found no significant reduction in the size of the lesions between patients treated with calcitonin therapy and the placebo group. Merritt et al. (2015) reported a case of juvenile ossifying fibroma of the mandible which was managed with calcitonin therapy however the lesion continued to progress and spread into both orbits despite this intervention. The authors concluded that calcitonin therapy was not effective in the management of such lesions.

2.9. Prognosis and recurrence

Prognosis is generally excellent while recurrence rate is estimated to range between 0 and 28% of cases (Sciubba and Younai 1989; Zachariades et al. 1984; Liu et al. 2010). Meister and co-workers (1973) reported on four patients with OF that were followed up for 18 years following surgical removal and it was reported that all cases had recurred.

In cases where the lesion recurred, then radical resection was indicated (Triantafillidou et al. 2012). Radiotherapy is not advised as these lesions are benign in nature and radio-resistant. There is also the possibility of subsequent malignant bone formation following radiotherapy (Mayo and Scott 1988). It is recommended that the clinician should follow-up these patients yearly (Triantafillidou et al. 2012).
2.10. **Juvenile ossifying fibroma**

Juvenile ossifying fibroma (JOF) is a subtype of OF that usually occurs within the maxillo-facial region of children below the age of 15 years (Liu et al. 2010). It is an uncommon and debated lesion that is differentiated from its adult variant on the basis of age, site, behaviour and microscopic features. JOF affected the maxilla more frequently than the mandible and may display signs of erosion and invasion of the adjacent bone structure accompanied by rapid enlargement (Noffke, 1998). It has a distinct histological presentation which includes a cell-rich fibrous stroma comprising bands of cellular osteoid with the absence of osteoblastic lining, osteoid strands and cement particles (Keles et al. 2010).

JOF is divided into 2 separate categories: the trabecular and the psammomatoid types. Trabecular JOF is identified by the occurrence of trabeculae and fibrillar osteoid and woven bone. The psammomatoid type is identified by the presence of small uniform spherical ossicles that mimic psammoma bodies (Slootweg et al. 1994).

The management and prognosis of JOF is uncertain. In some cases, it may occur with minimal symptoms, while in other cases, especially in very young patients, it may present with local aggressive behaviour. Therefore, due to the aggressive nature of these tumours with the high recurrence rate (30-58%), it is recommended that these locally aggressive neoplasms be treated with surgical resection rather than conservative curettage (El Mofly, 2002; Noffke, 1998).
2.11. Association of ossifying fibroma with giant cell lesions

A number of cases have been reported in the literature describing association of OF with other giant cell lesions of the jaws, including aneurysmal bone cyst (ABC) and central giant cell granuloma (CGCG) (Triantafillidou et al. 2012). This close association between the two lesions may be a reaction to a stromal change within the original lesion. It is thought that OF is usually the primary lesion and through some yet unidentified trigger, the tumour’s mesenchymal spindle cells release cytokines that trigger differentiation toward osteoclast giant cells (Triantafillidou et al. 2012).

El Deeb et al. (1980) reported that 21% of ABCs in the jaws were associated with other bone lesions. Trent and Byl (1993) reported an association between ABCs and bone lesions in 12% of cases, while, Padwa et al. (1997) found that 22% of all jaw ABCs described in the literature were related with another bone lesion, such as fibrous dysplasia, ossifying fibroma, or giant cell tumour.

It is believed that ABC may be a result of a haemorrhagic “blow out” of a pre-existing bone lesion. The original lesion may remain intact or may be completely destroyed (Triantafillidou et al. 2012). Martinez and Sissons (1988) reported that the incidence of ABC and another bony lesion in the jaws was more frequent in widely resected lesions than in curetted specimen.

2.12. Synchronous ossifying fibroma

Incidence of multiple synchronous OFs in the jaws is rarely reported in the literature. Only eighteen cases of synchronous OFs have ever been reported. The first case of synchronous OFs was reported by Bradley and Leake (1968). In 1989, Yih et al.
described multiple familial OFs as a heritable disorder. Khanna and Andrade (1992) described a case which presented with two OFs involving the maxilla and mandible. Hwang et al. (2001) reported on a rare case of a patient with multiple OFs in all four quadrants over a period of 18 years which lead to severe facial deformity and orbital compression. The majority of synchronous OFs in the reported literature occurred in females (85.7%). The mean age of the affected patients was 27.85 years (ranging from 6 to 37 years).

The incidence of synchronous OFs in the jaws has been linked with hormonal imbalances, such as hypercalcemia associated with hyperparathyroidism. Hyperparathyroidism– jaw tumour syndrome (HPT-JT) is an inherited autosomal dominant syndrome which can cause several or recurrent OFs of the jaws. This disorder is characterized by the development of parathyroid adenomas or carcinomas, fibro-osseous lesions of the jaws, renal disorders and pancreatic adenocarcinoma (Yamashita et al. 2007).

This unusual entity of multiple ossifying fibromas present in a single patient shows the possible variation in clinical, radiographic and histopathologic presentation and highlights the possibility of high recurrence rates of this lesion following surgical management.
Chapter 3

AIM AND OBJECTIVES

3.1. Aim

The aim of this study is to determine the demographic and radiological features of ossifying fibroma presenting at the Department of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology, University of the Western Cape Oral Health Centre as well as its management and recurrence patterns.

3.2. Objectives

1) To describe the demographic information of ossifying fibroma.
2) To describe the presenting radiographic features of ossifying fibroma.
3) To compare the demographic and radiological features of ossifying fibroma with other fibro-osseous lesions.
4) Analyze treatment methods and recurrence rates.
Chapter 4

MATERIALS AND METHODS

4.1. Study design

This was a retrospective case-series descriptive study of ossifying fibroma of the jaws. It was designed to study the clinical and radiographic features of this fibro-osseous lesion as well as its management and recurrence patterns during a period of forty years from 1976 to 2014.

4.2. Study sample

The sample for this study was selected by manually collecting all patient records available at the Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology of the University of the Western Cape Oral Health Centre in Cape Town, South Africa. All cases of ossifying fibroma included in this study were confirmed by histopathological and clinical findings prior to the inclusion in this study. All pathologic specimens were evaluated by Oral and Maxillofacial pathologists.

4.3. Selection criteria

Inclusion criteria for this study included:
Patient’s record with a histologically confirmed diagnosis of ossifying fibroma.

Patient’s record should be complete with all demographic and clinical data.

Presence of at least one pantomograph for each record

Exclusion criteria for this study included:

- Patients with unknown history or incomplete record
- Patient’s record with inconclusive diagnosis, either due to an insufficient biopsy specimen or inadequate clinical data.
- A patient panoramic radiograph with poor or insufficient diagnostic quality.

4.4. Data collection

All data collected for this study was recorded on a Microsoft Excel spreadsheet (Appendix 1). The data spreadsheet was formulated based on the objectives set out for this study. The data recorded included the patient’s age, gender and ethnicity. The clinical signs and symptoms of the lesion as well as the history were analyzed. Radiographic features including size, shape, margins, radio-density, location, locularity and its effect on adjacent structures (adjacent dentition, Inferior Alveolar nerve and/or Antrum) were noted. Management and follow-up were also documented.

4.5. Radiographic examination

All radiographs were examined by the same two pre-calibrated observers (principal investigator and study supervisor). Each image available for the study was examined
independently by each observer followed by comparison of the results. In cases where there is a disagreement of the findings amongst the two observers, then a third observer was consulted and the final decision was taken by consensus.

The panoramic radiographs used in this study were taken with a GE-3000 (General electric, Milwaukee, WI) or Cranex Tome CEPH (Soredex, Helsinki, Finland). All radiographs examined in this study were observed on a bright and evenly illuminated light-reflecting radiograph viewing box in an enclosed room with no light entry. This was done to standardise the setting for analysing the radiographs.

The viewing box was positioned in a comfortable position for the investigator. Adjunctive tools such as magnifying glasses were utilized to allow for detailed examination of the radiographs.

The location of the lesion was categorized into different regions in the mandible and maxilla. The anterior region of the mandible extended from the left canine (33) to right canine (43) and in edentulous patients from the left to right mental foramina. The posterior region of the mandible extended from canine to the angle of the mandible, for both left and right sides. The anterior region of the maxilla extended from the left canine (23) to right canine (13) while the posterior region of the maxilla extended from canine to the maxillary tuberosity.

The size of the lesion was measured in centimeters along the widest diameter of the lesion from one border to the opposite border. Radio-density was classified as either radio-lucent, radio-opaque and mixed (radio-lucent and radio-opaque in appearance). Lesions were further classified as either unilocular in appearance whereby only one compartment is present or multilocular whereby the lesion appears to be formed of many adjacent compartments within the bone.
The dentition affected by the lesion was recorded to demonstrate the extent of the lesion and whether it crosses the midline. The effect of the lesion on the cortex of the mandible was also noted to determine the expansive nature of the lesion. Signs of root resorption were also documented to demonstrate the aggressive nature of the lesion.

### 4.6. Data analysis

Data was analyzed using Epi Info® 2000 by student's unpaired t-test to compare the findings and to correlate these findings with different parameters such as age, gender, ethnicity, etc. Excel worksheet was used to collect the data and calculate averages, etc.

### 4.7. Ethical considerations

This was a retrospective case analysis of patient records from Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology, University of the Western Cape Oral Health Centre. Permission was obtained from the departments prior to commencement of the study.

No identifiable patient data was recorded such as their name or date of birth. Only the patient’s record number was noted for reference purposes. All records were stored on a password protected computer. Printed information was also stored in a locked office. All personal identifiers were changed when the data will be published.

In a case where clinical photographs are used to display a lesion, the patient’s identity was hidden and consent was obtained from the patient prior to publication of those photographs.
The research protocol for this study was presented to the Faculty of Dentistry of the University of the Western Cape research committee and was also approved by the Senate Research Ethics Committee (approval number: 15/6/84) of the University of the Western Cape.
A total 72 cases were diagnosed with ossifying fibroma from 1976 to 2014 at the Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology, University of the Western Cape Oral Health Centre. Of these cases, only 61 records had complete demographic information and radiographs. The other cases were excluded from this study.

5.1. Demographic data

The ages of patients at time of diagnosis ranged from 6 to 63 years with a mean age of 27.50 years for this sample. The most affected age group in this sample was 11 years to 20 years group with 14 patients (Table 3). Majority of patients were below 40 years of age (73.9%) at the time of diagnosis.

The majority of patients in this population were females (63.9%) with a male to female ratio of 1:1.7. It was noted that this lesion occurred more frequently in males in age groups below 10 years of age (80% of the age group) while it occurred more commonly in females when it presented in patients above 40 years of age (87.5% of the age group).
Table 3: Distribution of ages and gender of patients diagnosed with ossifying fibroma.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. patients</th>
<th>Percentage</th>
<th>No. Females</th>
<th>No. Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>10</td>
<td>16.4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>11-20</td>
<td>14</td>
<td>23.0</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>21-30</td>
<td>9</td>
<td>14.8</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>31-40</td>
<td>12</td>
<td>19.7</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>41-50</td>
<td>11</td>
<td>18.0</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>51-60</td>
<td>4</td>
<td>6.5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>61-70</td>
<td>1</td>
<td>1.6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>100</td>
<td>39</td>
<td>22</td>
</tr>
</tbody>
</table>

With regards to ethnicity of patients, most patients were of mixed race (65.57%) while Caucasians were the least affected by this condition with only 7 cases (11.47%). It was noted that the lesion occurred more commonly in patients of mixed race in the above 40 years age group (75%). By far, the most affected group of patients with ossifying fibroma were females of mixed race who formed 45.9% of the entire sample.

5.2. Clinical presentation

Many ossifying fibromas in this sample were discovered incidentally on pantomographs during prosthodontic examination. Nearly half of the cases in this sample were
symptomatic (49.2%) with an average period of 22 months from first symptoms to presentation. Table 4 shows the most common presenting sign and symptoms of patients in this sample. Swelling was the most frequent complaint (Figures 1 and 2).

**Table 4:** List of signs and symptoms in this sample.

<table>
<thead>
<tr>
<th>Sign &amp; Symptoms</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling</td>
<td>30</td>
<td>49.2%</td>
</tr>
<tr>
<td>Pain</td>
<td>9</td>
<td>14.7%</td>
</tr>
<tr>
<td>Mobile dentition</td>
<td>7</td>
<td>11.5%</td>
</tr>
<tr>
<td>Displaced dentition</td>
<td>16</td>
<td>26.2%</td>
</tr>
</tbody>
</table>

**Figure 1:** Clinical photograph of a young patient showing marked facial asymmetry.
5.3. Location

The mandible was the most affected jaw with 47 lesions (74.6%) while only 16 lesions (25.4%) occurred in the maxilla. The mandibular posterior region was most affected with 35 lesions (55.5%) while the maxillary anterior region was the least affected with only three cases (Figure 3). Interestingly, most lesions in patients below 10 years of age occurred in the mandibular posterior regions (80%).

Figure 2: Intra-oral image showing ossifying fibroma in right mandible presenting with marked swelling and buccal expansion.
There were 19 cases (30.2%) of ossifying fibroma that occurred in edentulous patients while 4 cases (6.3%) extended to the condyle in the mandible. Seven cases (11.1%) crossed the mid-line.

5.4. Radiographic features

5.4.1. Radio-density

Approximately half (49.2%) of the lesions in this study appeared as radio-opaque on pantomographs (Figure 4). While mixed (radio-lucent and radio-opaque) lesions were less frequent (34.92%) and radio-lucent lesions were least frequent (15.88%). Radio-opaque lesions were significantly more frequent in the older age groups (40 year and
above) than in younger patients ($P < 0.0001$). On the other hand, mixed density lesions were more common in patients of younger age groups (10 to 30 years).

![Figure 4: Pantomograph showing radio-opaque ossifying fibroma in the right mandible.](image)

5.4.2. Shape

The shape of ossifying fibroma has been described as round, oval or irregular on radiographs. The majority of lesions in this case series were irregular in shape (52.4%) (Figure 5) followed by round shape (41.26%) while oval shape (6.34%) was least prevalent.
Figure 5: Pantomograph showing irregular shape of ossifying fibroma in the right maxilla.

5.4.3. Locularity of lesion

Most lesions (84.1%) appeared as unilocular on pantomographs (Figure 6) while only 10 cases (15.9%) appeared as multilocular lesions. All multilocular lesions occurred exclusively in the mandibular posterior region. Eight out of these 10 multilocular lesions occurred in patients below 20 years of age. This finding was statistically significant ($P < 0.0001$).
5.4.4. Margins of lesion

Majority of lesions presented with well-defined margins (93.6%) and were easily identifiable from healthy surrounding bone (Figure 7). Only four lesions presented with ill-defined margins which all occurred in younger individuals.

Figure 6: Pantomograph showing unilocular ossifying fibroma in the right mandible.

Figure 7: Pantomograph showing well-defined ossifying fibroma in left mandible.
5.4.5. Effect on lamina dura

The lamina dura of dentition in close relation with ossifying fibromas were not affected in 54% of cases. In 29 cases (46%), the lamina dura was not present (Figure 8). The lamina dura was affected in most age groups (Mean = 24 years) in lesions with differing radio-densities.

![Figure 8: Lateral oblique radiograph of lesion showing loss of lamina dura.](image)

5.4.6. Root resorption

Most cases in this series did not show signs of root resorption. There were only eight cases (12.7%) that showed signs of root resorption on the dentition in close proximity to the lesion (Figure 9). Most cases with root resorption occurred in well-defined, multilocular lesions (62.5%) in younger patients (mean age = 18 years).
Figure 9: Pantomograph showing root resorption of the left mandibular first premolar and canine which are closely associated with ossifying fibroma.

5.4.7. Displacement of adjacent structures

Ossifying fibroma has the tendency to enlarge and cause displacement of different structures in the jaws including dentition, Inferior Alveolar canal and maxillary sinus. In this study, 23 cases (36.5%) displaced the adjacent dentition, 15 out of 41 mandibular posterior cases (36.5%) displaced the inferior alveolar canal (Figure 10) and 4 out of 13 maxillary posterior cases (30.8%) displaced the maxillary sinus.
Figure 10: Pantomograph showing displaced dentition and Inferior Alveolar canal due to ossifying fibroma on left side of mandible.

5.4.8. Size of lesions on pantomographs

The lesions were measured on pantomographs along their longest diameter to determine the extent of growth. The size of lesions ranged from 10 mm to 150 mm with an average size of 47.8 mm.

On average, mandibular lesions (51 mm) were considerably larger in size than maxillary lesions (38.1 mm). However, this difference did not show a statistical significance ($P = 0.23$) (Appendix 2). On the other hand, multilocular lesions (mean size = 96 mm) were significantly ($P < 0.0001$) larger in size than unilocular lesions (mean size = 39mm)
5.5. Initial Diagnosis

An initial clinical diagnosis made by the examining clinician was available in 24 cases. The initial clinical diagnosis of this lesion included ameloblastoma, cementoma, fibrosarcoma, osteosarcoma, central granuloma and radicular cyst. Five cases (20.8%) were initially diagnosed as ossifying fibroma. The most frequent initial diagnosis of this lesion was fibrous dysplasia. This was especially true for all cases that occurred in the maxilla and appeared radio-opaque on radiographs. This further highlights the similarities in presentation between ossifying fibroma and fibrous dysplasia.

5.6. Management

An incisional biopsy was performed on large, ill-defined lesions which could not be removed completely on initial biopsy. Excisional biopsy was done in small, well-defined, unilocular lesions whereby the entire lesion could be removed definitively from the affected site. Once definitive diagnosis of the lesion was established, a surgical approach was appropriately selected depending on the size, location, age, accessibility, locularity, invasion of adjacent structures and nature of the lesion. Surgical methods used to manage ossifying fibroma included enucleation, curettage and resection with reconstruction of the surgical site. Enucleation was only used on radio-lucent, unilocular cyst-like lesions (Figures 11 and 12). Most cases were managed by curettage (68.2%) where the lesion was excised from the surrounding normal bone. Younger patients with juvenile ossifying fibroma (4 cases) were treated with surgical resection of the lesion due to the aggressive nature of this lesion (Figures 13 and 14).
**Figure 11:** Pantomograph showing initial presentation of unilocular, radio-lucent ossifying fibroma in right mandible.

**Figure 12:** Pantomograph of same patient above following enucleation of lesion and packing of bismuth iodoform paraffin paste (BIPP).
**Figure 13:** Pantomograph showing initial presentation of ossifying fibroma in left maxilla.

**Figure 14:** Pantomograph of the same patient above following resection of lesion in left maxilla.
5.7. Recurrence

Patients’ records were examined for follow-up visits at the Department of Maxillo-Facial and Oral Surgery, University of the Western Cape. Following surgical treatment of this lesion and discharge from the department, patients were advised to attend a yearly follow-up to assess for any recurrences. Follow-up records were available for 22 patients with the follow-up period ranging from 3 months to 6 years. An average follow-up period for this sample was 20 months (Table 5). Only one case recurred in a middle-aged male initially presenting with a multilocular lesion. The lesion was initially managed with curettage and recurred six years following initial surgical management.

Table 5: Table showing surgical methods and recurrence rates for each method.

<table>
<thead>
<tr>
<th>Surgical Method</th>
<th>No. of Patients</th>
<th>Percentage</th>
<th>No. of Recurrences</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enucleation</td>
<td>3</td>
<td>13.6%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Curettage</td>
<td>15</td>
<td>68.2%</td>
<td>1</td>
<td>6.7%</td>
</tr>
<tr>
<td>Resection</td>
<td>4</td>
<td>18.2%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>100%</td>
<td>1</td>
<td>6.7%</td>
</tr>
</tbody>
</table>

5.8. Juvenile ossifying fibroma

In this study, there were seven cases diagnosed with juvenile ossifying fibroma (JOF). All patients were below the age of 13 years. Four patients were males while 3 were
females. Six lesions occurred in the mandible posterior regions (85.7%) while only one case presented in the anterior maxilla. Patients presented with considerably more swelling and pain than their older counterparts. All JOF lesions caused displacement of adjacent dentition. On radiographs, the majority of lesions were multilocular (71.4%), radio-lucent (57.1%) and well-defined (85.7%) (Figure 15). The size of JOF lesions on radiographs was significantly larger than other lesions ($P < 0.001$) which further highlight the aggressive nature of this lesion. Four cases of JOF were managed by resection with no record of any recurrences.

![Figure 15: Pantomograph showing juvenile ossifying fibroma in left mandible.](image)

**5.9. Synchronous ossifying fibroma**

There were two cases of multiple ossifying fibromas occurring in the same patient. Both cases occurred in middle-aged females. One patient was of caucasian origin while other
one was of mixed race. In both cases, the mandible was affected and lesions were small in diameter and round in appearance. All lesions in these two patients were radiopaque and unilocular.

In one case, the patient was edentulous (Figure 16) and the lesions were discovered incidentally while in the other, the lesions were associated with left and right mandibular first molars and were symptomatic. The latter case was treated by extraction of the associated dentition and curettage of the lesion. The patient returned for follow-up after 16 months from treatment and no recurrence was reported.

**Figure 16:** Pantomograph showing multiple ossifying fibromas in left and right sides of mandible.
Chapter 6

DISCUSSION

In this study, the clinical and radiological features of 61 patients presenting with ossifying fibroma at Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology at University of the Western Cape Oral Health Centre were analysed. The management and recurrence of this lesion were also examined. This is one of the largest case series to report on this lesion in the literature and one of the first comprehensive studies of its kind in a South African population group.

Comparison of the findings in this study with other population based studies revealed many similarities and some differences from other reports in the literature which are discussed in detail.

6.1. Epidemiology

The majority of previous studies reported in the literature were conducted in North American, Chinese and European populations. Few studies were conducted in Nigerian population groups while three studies were previously done in South Africa (Schmaman et al. 1970; Van Heerden et al. 1989; Ojo et al. 2014). The number of patients included in previous studies ranged from numerous single case studies to the largest study to date on ossifying fibroma which included 134 patients in a Japanese group (Matsuzaka et al.)
2002). This study is by far the largest in an African population group reported in the literature.

6.2. Age

The mean age of patients in this study was 27.5 years. Numerous authors such as MacDonald-Jankowski (1998) and Eversole et al. (1985) reported that the mean ages of patients affected by this lesion were higher compared to other populations. This finding was also supported by MacDonald-Jankowski and Li (2009) which reported that the mean ages from American, Asian and Latin American groups were greater than those reported for African group. This observation was confirmed by the results of this study as the mean age in this sample was one of the lowest as compared to the total of all studies reported in the literature which was 32 years. This discrepancy in the mean age of patients in different groups may be due to variations in the race of patients and the sample size.

It is well documented that the lesion occurs most frequently in patients below the age of 40 years (MacDonald-Jankowski 2009). In this sample, this was also the case with 73.9% of patients were below 40 years old. The most affected age group in this sample was 11-20 years group, meanwhile MacDonald-Jankowski (2009) in a systematic review demonstrated that the most frequently affected age group globally is 20-39 years. This difference in age at the time of presentation could be to the fact that this lesion occurs in younger patients in Africans when compared to other population groups.
6.3. Gender

There is a definite predilection of this lesion for females with reported rates of around 70% of all cases. This was also the finding in this study with 63.9% of patients being females. The exception is the two reports from Hong Kong in which all cases occurred in females (MacDonald-Jankowski 1998; MacDonald-Jankowski and Li 2009).

6.4. Clinical presentation

Swelling in the involved area is the most frequent clinical sign present in patients with OF. A number of patients with OF do not present with symptoms and the lesion is incidentally discovered on routine radiographic examination (de Andrade et al. 2013). Ossifying fibroma in Asian populations were seen to present with considerably more swellings, while in Africans, the lesion does not present with as much swelling in the affected jaw (MacDonald-Jankowski 2009). Studies by Mohanty et al. (2014), Triantafillidou et al. (2012), Sopta et al. (2011), Adekeye et al. (1980) and Anand et al. (1967) all reported that their entire study group (100% of the sample) presented with swelling associated with this lesion where as in this sample only 49.2% of the patients presented with swelling (Table 6). The average percentage of swelling associated with this lesion from all studies reported in the literature was 69.7% (Table 6). This sampled showed a lesser frequency of swelling associated with ossifying fibroma than in the reported literature. This difference could once again be attributed to genetic and environmental factors between the two population groups.
Table 6: Comparison of clinical presentation of ossifying fibroma in this population with previous reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Swelling</th>
<th>Pain</th>
<th>Mobile dentition</th>
<th>Displaced dentition</th>
<th>Duration of symptoms (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>30 (49.2%)</td>
<td>9 (14.7%)</td>
<td>7 (11.5%)</td>
<td>16 (26.2%)</td>
<td>22</td>
</tr>
<tr>
<td>Mohanty <em>et al.</em> (2014)</td>
<td>25 (100%)</td>
<td>9 (36%)</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td>20.5</td>
</tr>
<tr>
<td>de Andrade <em>et al.</em> (2013)</td>
<td>4 (50%)</td>
<td>1 (12.5%)</td>
<td>INA</td>
<td>1 (12.5%)</td>
<td>37</td>
</tr>
<tr>
<td>Triantafillidou <em>et al.</em> (2012)</td>
<td>14 (100%)</td>
<td>1 (7%)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>Sopta <em>et al.</em> (2011)</td>
<td>10 (100%)</td>
<td>6 (60%)</td>
<td>INA</td>
<td>3 (30%)</td>
<td>10.4</td>
</tr>
<tr>
<td>Liu <em>et al.</em> (2010)</td>
<td>19 (95%)</td>
<td>1 (5%)</td>
<td>9 (45%)</td>
<td>6 (30%)</td>
<td>37.6</td>
</tr>
<tr>
<td>MacDonald-Jankowski and Li (2009)</td>
<td>8 (33.3%)</td>
<td>3 (12.5%)</td>
<td>1 (4.1%)</td>
<td>6 (25%)</td>
<td>38</td>
</tr>
<tr>
<td>Chang <em>et al.</em> (2008)</td>
<td>26 (96%)</td>
<td>11 (39.3%)</td>
<td>0</td>
<td>5 (17.8%)</td>
<td>36</td>
</tr>
<tr>
<td>MacDonald-Jankowski (1998)</td>
<td>6 (30%)</td>
<td>3 (15%)</td>
<td>INA</td>
<td>3 (15%)</td>
<td>INA</td>
</tr>
<tr>
<td>Yoon <em>et al.</em></td>
<td>13 (81.2%)</td>
<td>2 (12.5%)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>Study</td>
<td>Pain Present</td>
<td>Mobile Dentition</td>
<td>Total</td>
<td>Published Year</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>------------------</td>
<td>-------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>Agrestini <em>et al.</em> (1987)</td>
<td>3 (50%)</td>
<td>3 (50%)</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iwasa and Soda (1980)</td>
<td>10 (83.3%)</td>
<td>2 (16.7%)</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adekeye <em>et al.</em> (1980)</td>
<td>7 (100%)</td>
<td>0</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sakota (1977)</td>
<td>27 (96.4%)</td>
<td>3 (10.7%)</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anand <em>et al.</em> (1967)</td>
<td>19 (100%)</td>
<td>6 (30%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total**: 191 (67.9%) 51 (19.2%) 11 (13.2%) 43 (27.4%) 28.6

INA: Information not available. NB: totals do not include data from this sample so as to allow comparison of results from this sample with the combined data available in the literature.

Pain associated with this lesion is a less frequent clinical presentation most likely due to the slow growing nature of this lesion. Agrestini *et al.* (1987) reported the highest rate of pain in any sample with 50% of their sample presenting with pain. The average rate of pain associated with this lesion for all reports in the literature was 19.2% or about one in every five patients presenting with ossifying fibroma. This sample once again showed lower frequency of pain associated with this lesion (14.2%) than other reported studies.

Mobile dentition associated with OF were a less frequent symptom reported in the literature. The mean frequency for this symptom was 13.2% from 4 reports which
included this detail in their finding. This was similar to what was found in this sample (11.5%)

6.5. Site

According to MacDonald-Jankowski (2009), ossifying fibroma presents almost equally in the maxilla and mandible in African populations while data from Asian, American and European populations show the mandible is near four times more frequently involved than the maxilla. This was not found to be the case in this sample as the majority of lesions occurred in the mandible (74.6%). The reason behind this finding could be due to the lack of previous data available on this lesion in Africa in the literature and the relatively small samples used in the systematic review for African populations.

The majority of studies in the literature agree that the mandibular posterior region in the most commonly affected site by ossifying fibroma (Table 7). Data from this sample showed similar finding as previously reported with 61.5% of cases involving the posterior region of the mandible. Meanwhile, American and European studies show that the anterior region of the mandible is the most frequently involve site (MacDonald-Jankowski 2009).
Table 7: Comparison of age and location of ossifying fibroma in this population with previous reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Maxilla: Mandible ratio</th>
<th>Maxilla Anterior</th>
<th>Maxilla Posterior</th>
<th>Mandible Anterior</th>
<th>Mandible Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>16:45</td>
<td>3 (5.2%)</td>
<td>13 (22.8%)</td>
<td>6 (10.5%)</td>
<td>35 (61.5%)</td>
</tr>
<tr>
<td>Mohanty et al. (2014)</td>
<td>6:19</td>
<td>4 (16.7%)</td>
<td>1 (4.2%)</td>
<td>0</td>
<td>19 (79.1%)</td>
</tr>
<tr>
<td>Ojo et al. (2014)</td>
<td>19:45</td>
<td>11 (17.2%)</td>
<td>8 (12.5%)</td>
<td>10 (15.6%)</td>
<td>35 (54.7%)</td>
</tr>
<tr>
<td>de Andrade et al. (2013)</td>
<td>1:7</td>
<td>1 (12.5%)</td>
<td>0</td>
<td>4 (50%)</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Hunasgi and Raghunath (2012)</td>
<td>9:16</td>
<td>2 (8%)</td>
<td>7 (28%)</td>
<td>4 (16%)</td>
<td>12 (48%)</td>
</tr>
<tr>
<td>MacDonald-Jankowski and Li (2009)</td>
<td>4:20</td>
<td>1 (4.5%)</td>
<td>3 (13.6%)</td>
<td>6 (27.4%)</td>
<td>12 (54.5%)</td>
</tr>
<tr>
<td>Chang et al. (2008)</td>
<td>2:26</td>
<td>0</td>
<td>2 (7.1%)</td>
<td>3 (10.7%)</td>
<td>23 (82.2%)</td>
</tr>
<tr>
<td>Olgac et al. (2006)</td>
<td>9:30</td>
<td>3 (7.7%)</td>
<td>6 (15.4%)</td>
<td>5 (12.8%)</td>
<td>25 (64.1%)</td>
</tr>
<tr>
<td>Ogunsalu et al. (2001)</td>
<td>5:3</td>
<td>2 (28.5%)</td>
<td>2 (28.5%)</td>
<td>1 (14.5%)</td>
<td>2 (28.5%)</td>
</tr>
<tr>
<td>Study</td>
<td>Ratio</td>
<td>Stage 1</td>
<td>Stage 2</td>
<td>Stage 3</td>
<td>Stage 4</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>MacDonald- Jankowski (1998)</td>
<td>3:17</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
<td>7 (35%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Mosqueda- Taylor <em>et al.</em> (1997)</td>
<td>4:1</td>
<td>1 (20%)</td>
<td>3 (60%)</td>
<td>0</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Yoon <em>et al.</em> (1989)</td>
<td>5:11</td>
<td>2 (12.5%)</td>
<td>3 (18.7%)</td>
<td>2 (12.5%)</td>
<td>9 (56.3%)</td>
</tr>
<tr>
<td>Sciubba and Younni (1989)</td>
<td>4:14</td>
<td>1 (5.5%)</td>
<td>3 (16.7%)</td>
<td>3 (16.7%)</td>
<td>11 (61.1%)</td>
</tr>
<tr>
<td>Eversole <em>et al.</em> (1985)</td>
<td>7:57</td>
<td>4 (6.3%)</td>
<td>3 (4.7%)</td>
<td>46 (71.9%)</td>
<td>11 (17.1%)</td>
</tr>
<tr>
<td>Iwasa and Soda (1980)</td>
<td>1:11</td>
<td>0</td>
<td>1 (9%)</td>
<td>0</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>Langdon <em>et al.</em> (1976)</td>
<td>3:7</td>
<td>2 (20%)</td>
<td>1 (10%)</td>
<td>1 (10%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5:46</td>
<td>35 (9.7%)</td>
<td>45 (12.5%)</td>
<td>92 (25.5%)</td>
<td>189 (52.3%)</td>
</tr>
</tbody>
</table>

NB: totals do not include data from this sample so as to allow comparison of results from this sample with the combined data available in the literature.
6.6. Radiographic presentation

Conventional radiographs as well as advanced imaging modalities such as CT and CBCT scans assist in describing ossifying fibroma in terms of location, size, expansion of cortical plates, internal structure, borders of the lesion, and the effect on adjacent anatomical structures. Consequently, an accurate provisional diagnosis can be made prior to histopathological investigation. Imaging also plays a vital role in the selection of treatment method to best manage the lesion.

This study focuses mainly on conventional radiographs as the main method of radiographic examination of this lesion. The study was a retrospective study with records obtained from the archives. The radiographic records were all conventional radiographs.

Currently all bony lesions will receive advance imaging involving either CT or CBCT as part of the standard assessment protocol used in the Department of Maxillo-Facial and Oral Surgery at the University of the Western Cape.

Advanced imaging such as CT scans is valuable in determining the exact extent of the lesion and its internal architecture; however it’s costly and not widely available in the developing countries. MR imaging is of less value in the examination and management of this lesion as soft tissue involvement is rare in this lesion.

It can be argued that the study has value in the developing world because conventional radiographs are readily available, cost-effective, easy to interpret and provide good overall information about the lesion. Numerous studies in the literature have shown that conventional radiographs provide most of the information required to make a reasonably accurate provisional diagnosis and outline the extent of the lesion.
6.6.1. Radio-density

The radiographic presentation of OF described in the literature vary significantly. With regards to the radiological presentation of the lesion in this sample, it was noted that nearly half of all lesions appeared as radio-opacity. This was different to the predominant appearance reported in the literature of “radio-opacity within a radiolucency” or otherwise known as mixed lesion. Mixed lesions occurred only in 34.9% of patients in this study. On the other hand, MacDonald-Jankowski (2009) found that radio-lucency was the most frequent radiological presentation based on studies in African populations. The appearance of radio-lucent lesions in younger patients may indicate that calcification occur progressively with age (MacDonald-Jankowski 1998).

Enlargement of OF with time may led to an increase in the amount of mineralized material deposited into the lesion. This is called maturation of the tumour. However, according to certain authors, the use of the term “maturation” to describe this phenomenon in neoplastic lesions is controversial (Liu et al. 2010). From a biological point of view, neoplasms have an indefinite growth and do not mature. The term “maturation” should rather be reserved for dysplastic lesions such as osseous dysplasia (Noffke et al. 2012).

6.6.2. Shape

In a systematic review by MacDonald-Jankowski (2009), it was reported that ossifying fibroma in contrast to fibrous dysplasia presents as a well-defined lesion on radiographs and is oval or round in shape. But, in fact the majority of lesions in this sample presented as irregular in shape (52.4%). This especially noted when the lesion recurs or
develops rapidly in a short period of time. OF usually grows along the body of the jaws, and at times may involve the entire jaw. This behaviour of ossifying fibroma may indicate aggressive local growth pattern and may present as irregular in shape on radiographs (MacDonald-Jankowski 2009).

6.6.3. Locularity of lesion
Multilocular ossifying fibromas occurred in 20% of cases from the only three studies in the literature which included this information (Eversole et al. 1985; Sciubba and Younai 1989; MacDonald-Jankowski and Li 2009). A similar finding was observed in this sample with 15.9% of lesions presented with multilocular appearance.

6.6.4. Margins of lesion
According to MacDonald-Jankowski (1998), radiological diagnosis of OF is not difficult for Maxillofacial radiologists, however, in this study not all radiological diagnoses corresponded with the histological findings. In this sample, it was noted that there are two main radiographic patterns of presentation of OF namely: cystic lesion (unilocular or multilocular) and mixed-density lesion. The margins of lesion in this sample appeared fairly smooth, well-defined and frequently corticated. This was also reported by numerous other reports including de Andrade et al. (2013), Chang et al. (2008), Sciubba and Younni (1989) and Eversole et al. (1985).
6.6.5. Effect on lamina dura

Liu et al. (2010) reported that in the majority of patients affect by OF, the lamina dura is missing. This was also found to be the case in this sample as in more than half the cases (54%), the lamina dura was still absent. This was especially true for younger patients in this group.

6.6.6. Root resorption

Root resorption is thought to be directly linked to the aggressive nature of a lesion. Resorption of roots of dentition in close proximity to OF is a rare radiographic finding associated with this lesion. In this sample, only 13% of cases presented with root resorption mainly due to the benign, slow-growing nature of most lesions. The average rate of all studies in the literature for root resorption was found to be 21% (Table 8). Studies by de Andrade et al. (2013) and MacDonald-Jankowski (1998) were the only reports in the literature to note no root resorption occurred in any of their cases. On the other hand, Sciubba and Younai (1989) and Eversole et al. (1985) reported that 44% and 16%, respectively, of OF caused root resorption.

6.6.7. Displacement of adjacent structures

Tooth displacement in the reported literature as shown in Table 8 is present in 27.1% of all patients. A slightly higher rate of displacement of dentition was found in this sample (37%). This higher rate of displacement in this sample could be due to large and extensive lesions included in this study.
Lesions in this sample also displaced adjacent anatomical structures such as inferior alveolar canal in the mandible (15 cases, 36.5%) and maxillary antrum in the maxilla (4 cases, 30.8%). MacDonald-Jankowski and Li (2009) reported inferior alveolar canal involvement in 8 out of 13 cases (61.5%) in their sample. This was significantly higher than this sample. Antral involvement was reported by MacDonald-Jankowski and Li (2009) to be present in 12.5% of cases while Sciubba and Younai (1989) reported a 16.6% of cases involved the maxillary antrum which are lower than in this sample. These differences can once again be attributed to the size and position of the lesion included in these studies.

6.6.8. Size of lesions

Very few studies in the literature have reported on the size of OF on radiographs. MacDonald-Jankowski and Li (2009) reported in their sample of 24 Hong Kong patients the average size of lesions on Pantomographs to be 4.77 cm. In this sample, the mean size of lesion was very similar (4.78 cm). In another study by MacDonald-Jankowski (1998), the mean size was also found to be similar (3.91 cm) to this sample. On the other hand, Chang et al. (2008) reported a much lower mean size in their sample (1.9 cm).

These differences could be due to the sample size and the ages of patients and time period for which the lesion has been present. Generally, the longer the lesion is present in the jaws, the larger in size it will present. It has also been shown that patients with Juvenile OF presented with significantly larger lesions than the rest of the sample.
**Table 8:** Comparison of radiographic features of ossifying fibroma in this population with previous reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Lucent (%)</th>
<th>Opaque (%)</th>
<th>Mixed (%)</th>
<th>Well-defined (%)</th>
<th>Root resorption (%)</th>
<th>Tooth displacement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This Study</td>
<td>10 (16%)</td>
<td>31 (49%)</td>
<td>22 (35%)</td>
<td>59 (94%)</td>
<td>8 (13%)</td>
<td>23 (37%)</td>
</tr>
<tr>
<td>Mohanty <em>et al.</em> (2014)</td>
<td>14 (56%)</td>
<td>5 (20%)</td>
<td>6 (24%)</td>
<td>17 (68%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>de Andrade <em>et al.</em> (2013)</td>
<td>1 (12.5%)</td>
<td>1 (12.5%)</td>
<td>5 (62.5%)</td>
<td>8 (100%)</td>
<td>0</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Liu <em>et al.</em> (2010)</td>
<td>6 (30%)</td>
<td>3 (15%)</td>
<td>11 (55%)</td>
<td>INA</td>
<td>9 (45%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>MacDonald-Jankowski and Li (2009)</td>
<td>4 (16.7%)</td>
<td>2 (8.3%)</td>
<td>18 (75%)</td>
<td>INA</td>
<td>1 (4.2%)</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>Chang <em>et al.</em> (2008)</td>
<td>6 (21%)</td>
<td>5 (18%)</td>
<td>17 (61%)</td>
<td>28 (100%)</td>
<td>INA</td>
<td>5 (17.8%)</td>
</tr>
<tr>
<td>Ogunsalu <em>et al.</em> (2001)</td>
<td>1 (12.5%)</td>
<td>3 (37.5%)</td>
<td>4 (50%)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>MacDonald-Jankowski (1998)</td>
<td>4 (20%)</td>
<td>1 (5%)</td>
<td>15 (75%)</td>
<td>18 (90%)</td>
<td>0</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Su <em>et al.</em> (1997)</td>
<td>40 (53%)</td>
<td>30 (40%)</td>
<td>5 (7%)</td>
<td>64 (85%)</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>Study</td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
<td>12-14</td>
<td>15+</td>
<td>Total</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
<td>-------</td>
</tr>
<tr>
<td>Swaroop et al. (1990)</td>
<td>2 (25%)</td>
<td>5 (62.5%)</td>
<td>1 (12.5%)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>Sciubba and Younni (1989)</td>
<td>10 (56%)</td>
<td>1 (5%)</td>
<td>7 (39%)</td>
<td>18 (100%)</td>
<td>6 (44%)</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>Zhang (1989)</td>
<td>2 (13.3%)</td>
<td>12 (80%)</td>
<td>1 (6.7%)</td>
<td>INA</td>
<td>7 (46.7%)</td>
<td>11 (73.3%)</td>
</tr>
<tr>
<td>Eversole et al. (1985)</td>
<td>20 (31%)</td>
<td>11 (17%)</td>
<td>33 (52%)</td>
<td>64 (100%)</td>
<td>7 (11%)</td>
<td>11 (17%)</td>
</tr>
<tr>
<td>Zachariades et al. (1984)</td>
<td>2 (12.5%)</td>
<td>6 (37.5%)</td>
<td>6 (37.5%)</td>
<td>7 (43.7%)</td>
<td>2 (12.5%)</td>
<td>3 (18.7%)</td>
</tr>
<tr>
<td>Waldron and Giansanti (1973)</td>
<td>11 (25.6%)</td>
<td>5 (11.6%)</td>
<td>27 (62.8%)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>24%</strong></td>
<td><strong>23.1%</strong></td>
<td><strong>38.75%</strong></td>
<td><strong>68.7%</strong></td>
<td><strong>21.4%</strong></td>
<td><strong>27.1%</strong></td>
</tr>
</tbody>
</table>

INA: Information not available. NB: totals do not include data from this sample so as to allow comparison of results from this sample with the combined data available in the literature.

### 6.7. Juvenile ossifying fibroma

In a series of eight cases of JOF, Williams *et al.* (2000) reported that all patients in their sample were below 15 years of age. The lesion was more common in males (62.5%) than females. In this sample a similar finding was also noted in that males (57.1%) were more affected than females while all patients were below 13 years of age.
The majority of JOF in this sample presented in the mandible (85.7%) as was also reported by Williams et al. (2000) who noted 75% of lesions presented in the mandible and were most well-defined and multilocular. JOF in this sample were also mostly multilocular and well-defined.

Williams et al. (2000) reported that half the patients in their sample presented with recurrences following surgical management. No mention was made of the surgical methods used in their sample and the follow-up period. In this study, four cases had surgical and follow-up records. All four patients were treated with resection of lesion and reconstruction. No recurrences were recorded for these four patients following a mean follow-up period of 10 months. Hence, it is recommended that patients with JOF should be treated more radically due to higher recurrence rate and aggressive nature of this lesion.

6.8. Synchronous ossifying fibroma

The ratio of synchronous OF cases to solitary OF cases is unknown, however, in our sample, 2 cases were found in 61 patients presenting with OF (3.2%). Only 18 known cases of synchronous ossifying fibroma have been reported in the literature to date (Table 9).

The aetiology and pathogenesis of both solitary and synchronous OF remain unknown. However, both types of OF show very comparable clinical, radiographic and histological features hinting that they are different clinical presentations of the same lesion (Wang et al. 2014).
The mean age of patients affected by synchronous OF in all reports in the literature was 28.7 years while females (72.2%) were more commonly affected than males (Table). The two cases in this study both occurred in older females (mean age 40.5 years). The maxilla and mandible seem to be equally affected by synchronous OF from reports in the literature; however in this sample, all lesions occurred in the mandible. Radiographically, synchronous OF presented equally as radio-lucent (8 reports) and mixed density (8 reports) in the literature. In this sample, one patient presented with radio-opaque lesions bilaterally on mandible while the other patient presented with mixed density lesions also bilaterally on mandible.

Majority of synchronous OF cases in the literature were managed conservatively with enucleation or curettage while only one case underwent resection. In this sample, the only case with treatment record was managed with curettage. Four cases in the literature recurred while no recurrences were recorded in this study.

**Table 9:** Comparison of all studies on synchronous OF in the literature with this sample.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>M/F</th>
<th>Site</th>
<th>Radio. features</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>49</td>
<td>F</td>
<td>Les 1: R Mand&lt;br&gt;Les 2: L Mand</td>
<td>Radio-opaque</td>
<td>INA</td>
<td>INA</td>
</tr>
<tr>
<td>This study</td>
<td>32</td>
<td>F</td>
<td>Les 1: R Mand&lt;br&gt;Les 2: L Mand</td>
<td>Mixed</td>
<td>Curettage</td>
<td>No recurrence 1 year 4 months later</td>
</tr>
<tr>
<td>Authors</td>
<td>Age</td>
<td>Gender</td>
<td>Lesion 1</td>
<td>Lesion 2</td>
<td>Treatments</td>
<td>Outcome</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----</td>
<td>--------</td>
<td>-------------------------------</td>
<td>-------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Takeda and Fujioka</td>
<td>55</td>
<td>M</td>
<td>L Max</td>
<td>R Max</td>
<td>Mixed, INA</td>
<td>Refused treatment</td>
</tr>
<tr>
<td>(1987)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hauser et al.</td>
<td>35</td>
<td>M</td>
<td>R Max</td>
<td>L Max</td>
<td>Mixed, Enucleation</td>
<td>INA</td>
</tr>
<tr>
<td>(1989)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yih et al.</td>
<td>31</td>
<td>F</td>
<td>L Mand</td>
<td>R Max</td>
<td>Radio-lucent, Enucleation</td>
<td>Recurrence 2 years later</td>
</tr>
<tr>
<td>(1989)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Khanna and Andrade</td>
<td>33</td>
<td>M</td>
<td>R Max</td>
<td>L Mand</td>
<td>Mixed, Enucleation</td>
<td>Lost for follow-up</td>
</tr>
<tr>
<td>(1992)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hwang et al.</td>
<td>25</td>
<td>F</td>
<td>R Mand</td>
<td>L Max</td>
<td>Mixed, Partial resection</td>
<td>Recurrence 3 years later</td>
</tr>
<tr>
<td>(2001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bertolini et al.</td>
<td>37</td>
<td>F</td>
<td>L Max</td>
<td>R Mand</td>
<td>Radio-lucent, Curettage</td>
<td>No recurrence 2 years later</td>
</tr>
<tr>
<td>(2002)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barberi et al.</td>
<td>53</td>
<td>F</td>
<td>L Infra-orbit</td>
<td>R Max</td>
<td>Mixed, INA</td>
<td>INA</td>
</tr>
<tr>
<td>(2003)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stergiou et al.</td>
<td>36</td>
<td>F</td>
<td>L Mand</td>
<td>R Mand</td>
<td>Mixed, Enucleation and curettage</td>
<td>No recurrence 6 months later</td>
</tr>
<tr>
<td>(2007)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chindia et al.</td>
<td>27</td>
<td>F</td>
<td>R Mand</td>
<td>L Max</td>
<td>INA, Enucleation</td>
<td>Recurrence 6 months later</td>
</tr>
<tr>
<td>(2008)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribeiro et al.</td>
<td>35</td>
<td>F</td>
<td>L Mand</td>
<td>R Mand</td>
<td>Mixed, Enucleation</td>
<td>No recurrence 3 years later</td>
</tr>
<tr>
<td>(2011)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agarwal et al.</td>
<td>20</td>
<td>F</td>
<td>L Max</td>
<td>R Mand</td>
<td>Radio-lucent, INA</td>
<td>INA</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.9. Differentiation ossifying fibroma

Ossifying fibroma on radiographs can present similar to a number of lesions that typically show “ground glass” appearance. Differential diagnosis should include: fibrous dysplasia, osteitis deformans, hyperparathyroidism (Brown’s tumour) and diffuse sclerosing osteomyelitis. Fibrous dysplasia should be the main lesion in the list of differential diagnosis for ossifying fibroma (Triantafillidou et al. 2012). Ossifying fibroma and fibrous dysplasia represents a diagnostic dilemma for clinicians, radiologists and pathologists as they show very similar radiographic and histological features. On radiographs, fibrous dysplasia often appears as a homogeneous, diffuse, radio-opaque area with ground-glass appearance. On the other hand, OF usually appears as a well-defined mixed lesion on radiographs (McCarthy 2013). In a study by
Toyosawa *et al.* (2007), it was shown that ossifying fibroma and fibrous dysplasia could be identified from one another by conducting polymerase chain reaction analysis with peptide nucleic acid for GNAS mutations at the Arg201 codon.

Ossifying fibroma may present in hyperparathyroidism as with ground glass appearance on radiographs, this could be distinguished from ossifying fibroma based on elevated calcium and parathyroid hormone levels in the blood. On the hand, in cases of osteitis deformans, phosphorous and calcium could be normal in the blood, however alkaline phosphatase levels are exceedingly high. In some cases, diffuse sclerosing osteomyelitis may present as a mixed (radio-lucent and radio-opaque) lesion mimicking ossifying fibroma. This lesion can be distinguished from ossifying fibroma in that it lacks a defined border on Pantomograph, and is usually caused by a low grade infection which can be confirmed biopsy and anaerobic culture. On biopsy, it is further possible to differentiate diffuse sclerosing osteomyelitis from ossifying fibroma in that it contains reactive sclerotic bone lined by osteoblasts with no cementum-like calcifications present (Sopta *et al.* 2011). Ossifying fibroma can also be often confused with focal cement-osseous dysplasia due to a similar mixed (radio-lucent and radio-opaque) radiographic presentation. Focal cement-osseous dysplasia is classified as a reactive lesion and not a neoplasm. It usually presents apical to the roots of mandibular incisors and does not cause any expansion of bone. On the contrary, OF has the potential to behave aggressively leading to cortical expansion and displacement of dentition and other anatomical structures. Histologically, both lesions may display similar features with trabecular bone deposition and cementifying areas. Mature cement-osseous dysplasias may present with densely corticated bony islands, a feature that is not present in OF.
6.10. Surgical Management

The surgical management of OF depends mainly on its clinical and radiological presentation and usually entails one of the following methods namely, enucleation, curettage and resection. Small lesions are generally managed conservatively by curettage or enucleation, until healthy bony margins are reached. Larger lesions necessitate surgical resection of the entire segment (Brannon and Fowler 2001). Complete surgical removal of the lesion at the earliest possible stage has been advised by most authors (Kouri et al. 1995; Gondivkar et al. 2011).

Mandibular OFs are usually well-defined and can normally be curetted or enucleated with easy intra-operatively, however maxillary OFs are more challenging to excise completely than mandibular lesions. This is possibly due to the difference in characteristics of the bone between the maxilla and mandible and also due to the available space for expansion into the maxillary antrum (Gondivkar et al. 2011).

The majority of cases in this sample were treated by curettage (68.2%). Enucleation was the most widely used method in the literature (49.7%). Resection was the least widely used method in this sample (18.2%) and in the literature as well (13.7%)

Conservative surgical methods are the preferred treatment of choice of OF as they are less debilitating to the patient and the wound can either be closed primarily or left open to heal secondarily. Resection on the other hand is very debilitating for the patient as a section of the jaw is excised which leads to alter occlusion, aesthetic deformity and functional loss. The patient usually requires grafting of bone in the area following resection which means subsequent surgeries and higher cost (Mohanty et al. 2014).
6.11. Recurrence

According to data from the reported literature as shown in Table 10, an average recurrence rate of 10.1% can be calculated with an average follow-up period of 25.3 months. The highest recurrence rate was reported by Liu et al. (2010) of 27.2%, while both Mohanty et al. (2014) and Chang et al. (2008) reported no recurrences. MacDonald-Jankowski and Li (2009) followed up 15 patients with OF over a mean period of 63.7 months, which is the longest reported follow-up period in the literature, found that only one case recurred (recurrence rate: 6.7%). In this sample, only one case recurred (recurrence rate: 6.7%) following an average follow-up period of 20 months. This recurrence rate for this sample is below the reported average in the literature. However, the follow-up period in this sample was also lower than that reported in the literature mainly due to lack of patient compliance and inadequate record keeping.

Table 10: Comparison of management and recurrence of ossifying fibroma in this population with previous reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Enucleation</th>
<th>Curettage</th>
<th>Resection</th>
<th>Mean follow-up</th>
<th>No. of recurrence</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>3 (13.6%)</td>
<td>15 (68.2%)</td>
<td>4 (18.2%)</td>
<td>20</td>
<td>1</td>
<td>6.7%</td>
</tr>
<tr>
<td>Mohanty et al.</td>
<td>19 (76%)</td>
<td>2 (8%)</td>
<td>4 (16%)</td>
<td>20.5</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>(2014)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Cases</td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
<td>Other</td>
<td>Overall</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>---------</td>
<td>-------</td>
<td>---------</td>
</tr>
<tr>
<td>de Andrade et al. (2013)</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>62.5%</td>
</tr>
<tr>
<td>Triantafillidou et al. (2012)</td>
<td>11 (78.6%)</td>
<td>0</td>
<td>3 (21.4%)</td>
<td>30</td>
<td>2</td>
<td>14%</td>
</tr>
<tr>
<td>Liu et al. (2010)</td>
<td>2 (22.3%)</td>
<td>4 (44.4%)</td>
<td>3 (33.3%)</td>
<td>63.3</td>
<td>3</td>
<td>27.2%</td>
</tr>
<tr>
<td>MacDon ald-Jankowski and Li (2009)</td>
<td>INA</td>
<td>INA</td>
<td>INA</td>
<td>63.6</td>
<td>1</td>
<td>6.3%</td>
</tr>
<tr>
<td>Chang et al. (2008)</td>
<td>7 (25%)</td>
<td>17 (60.7%)</td>
<td>3 (10.7%)</td>
<td>INA</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Sciubba and Younai (1989)</td>
<td>2 (11.1%)</td>
<td>13 (72.2%)</td>
<td>2 (11.1%)</td>
<td>INA</td>
<td>1</td>
<td>5.5%</td>
</tr>
<tr>
<td>Eversole et al. (1985)</td>
<td>18 (78.2%)</td>
<td>0</td>
<td>0</td>
<td>38</td>
<td>5</td>
<td>21.8%</td>
</tr>
</tbody>
</table>
Zacharia des et al. (1984)  

|       | 14 (87.5%) | 0 | 2 (12.5%) | 18 | 1 | 6.2% |

Total  

|       | 76 (49.7%) | 56 (36.6%) | 21 (13.7%) | 25.3 | 14 | 10.1% |

INA: Information not available. NB: totals do not include data from this sample so as to allow comparison of results from this sample with the combined data available in the literature.

Eversole and co-authors (1985) reported a recurrence rate of 28% following enucleation and curettage of 22 patients affected by OF who were followed up over a period of 38 months. On the other hand, the time of recurrence was constantly unpredictable with reports in the literature ranging from 6 months to 7 years following surgical intervention (Liu et al. 2010). Consequently, Liu et al. (2010) recommended that there should be an extended follow-up period of 10 years. This reinforces the conclusions by Meister and co-authors (1973) of recurrence subsequent to long-term follow-up and emphasis the need for long-term follow-up of patients treated for OF.

It has been reported that recurrent OF frequently become larger in size or may present with an extensively altered radiographic appearance (Liu et al. 2010). It is believed that the surgery can reactivate the growth of a lesion. Some authors have reported that dental infection and tooth extractions may stimulate the periodontal membrane to form and deposit cementum (Hamner et al. 1968). There is sound possibility that trauma to the affected region could be a contributing factor in the proliferation of this lesion (Cheng et al. 2002; Brademann et al. 1997).
Based on the findings of this study and other reports in the literature, a surgical protocol has been drawn up to be aid in the surgical management of ossifying fibroma as shown in Table 11.

**Table 11: Proposed protocol for surgical management of ossifying fibroma.**

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Recommended cases for management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enucleation</td>
<td>• To be used in cases where the tumour is well defined, encapsulated, easily accessible and is small/medium in size.</td>
</tr>
<tr>
<td>Curettage</td>
<td>• To be used in cases there was no clear radiolucency around the tumour.</td>
</tr>
<tr>
<td></td>
<td>• In cases where the tumour is composed of soft bone which is fused with the surrounding normal bone on surgical exploration.</td>
</tr>
<tr>
<td></td>
<td>• Tumour could not be removed due to its size or inaccessibility.</td>
</tr>
<tr>
<td>Resection with reconstruction</td>
<td>• Resection is performed in tumours in close proximity or involving the inferior border of mandible.</td>
</tr>
<tr>
<td></td>
<td>• Tumours extending into the maxillary antrum and/or nasal cavities with ill-defined borders should also be managed with resection.</td>
</tr>
<tr>
<td></td>
<td>• Resection margins should not exceed 5 mm into normal bone margins as it is reported that the tumour does not infiltrate surrounding bone more than 1–2 mm.</td>
</tr>
</tbody>
</table>
LIMITATIONS OF THIS STUDY

Due to the retrospective design of this study, there could be no standardisation of the radiographic quality, as different panoramic machines were used with a variation of radiation exposure factors for each case at the time the radiographs were taken.

There was also the issue of lack of information in some cases. In certain cases, it was difficult to obtain the clinical sign and symptoms of the lesions especially for older cases where the patient’s record was missing or incomplete. Only radiographs and histopathological reports were present along with personal information in the archives of the Departments of Maxillo-Facial and Oral Surgery and Diagnostics and Radiology at the University of the Western Cape Oral Health Centre.

It was noted while reviewing radiographs in this study that the majority of patients were partially edentulous over the area where the lesions occurred. The cause for this observation could not be determined for certain but can be attributed to the fact that the lesion may have caused the overlying dentition to become mobile and warranted the extraction of the dentition. Another possible reason could be due to misdiagnosis of the swelling in the area for dental abscess and hence the teeth were extracted.

The lack of availability of advanced imaging modalities such CT, CBCT and MR imaging in this study sample could also be considered a limitation of this study. There few reports in the literature on advanced imaging of this lesion and hence inclusion of
such information in this study would have been valuable. The lack of availability of advanced imaging is mainly due to the high costs involved and lack of availability of such facilities. Also numerous cases in this sample were diagnosed with the lesion before the arrival of these advanced imaging facilities in public hospitals in South Africa.

Another limitation of this study could be the number of cases of Juvenile and synchronous ossifying fibroma. Although the number of ossifying fibroma cases is one of the largest in the literature, there were only limited numbers of Juvenile and synchronous ossifying fibroma. The sample of these two rare entities of ossifying fibroma is not significant to arrive at conclusion to confidently describe the presenting features of these lesions.

One final limitation of this study is the lack of the follow-up reports for many cases. A possible reason for this is the inability of patients to report for follow up appointments as many patient live long distances away from University of the Western Cape Oral Health Centre and cannot afford to travel.
Chapter 8

CONCLUSIONS

In conclusion, ossifying fibroma occurred frequently in females and in patients below 40 years of age with the mandibular posterior region being the most affected site. They have the tendency to grow into large size causing swelling and facial asymmetry along with pain and paraesthesia. They are usually well-defined, radio-opaque lesions that seldom infiltrate the surrounding tissues.

Surgical management in the form of enucleation, curettage and resection are suitable forms of treatment as shown in this study by a very low recurrence rate reported. Conservative curettage is the treatment of choice for small well-defined lesions while enucleation should be performed in fairly large lesions with defined borders. Resection should be employed for extensive lesions that behave aggressively. Long term follow-up of patients is mandatory as recurrences can occur for up to 10 years following treatment.
Chapter 9

REFERENCES


# APPENDIX 1

**Data Collection Sheet**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Library number</strong></td>
<td></td>
</tr>
<tr>
<td><strong>2. Age</strong></td>
<td></td>
</tr>
<tr>
<td><strong>3. Gender:</strong></td>
<td>M=1  F=2</td>
</tr>
<tr>
<td><strong>4. Race:</strong></td>
<td>Caucasian=1  African=2  Indian=3  Coloured=4</td>
</tr>
<tr>
<td><strong>5. Location:</strong></td>
<td>Mand Ant=1  Mand Post=2  Max Ant=3  Max Post=4</td>
</tr>
<tr>
<td><strong>6. Size (mm)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>7. Radio-density:</strong></td>
<td>opaque=1  mixed=2  lucent=3</td>
</tr>
<tr>
<td><strong>8. Margins of lesion:</strong></td>
<td>well-defined=1  ill-defined=2</td>
</tr>
<tr>
<td><strong>9. Loculation:</strong></td>
<td>unilocular=1  multilocular=2</td>
</tr>
<tr>
<td><strong>10. Dentition involved (teeth number)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>11. Expansion of cortex:</strong></td>
<td>yes=1  no=2</td>
</tr>
<tr>
<td><strong>12. Root resorption:</strong></td>
<td>yes=1  no=2</td>
</tr>
<tr>
<td><strong>13. Symptomatic:</strong></td>
<td>yes=1  no=2  <strong>Duration:</strong></td>
</tr>
<tr>
<td><strong>14. Time from initial symptoms to presentation</strong></td>
<td></td>
</tr>
<tr>
<td><strong>15. Initial diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td><strong>16. Management:</strong></td>
<td>enucleation=1  curettage=2  resection=3  none=4</td>
</tr>
<tr>
<td><strong>17. Recurrence:</strong></td>
<td>yes=1  no=2</td>
</tr>
<tr>
<td><strong>18. Juvenile Ossifying Fibroma:</strong></td>
<td>yes=1  no=2</td>
</tr>
<tr>
<td><strong>19. Synchronous (multiple) Ossifying Fibromas:</strong></td>
<td>yes=1  no=2</td>
</tr>
</tbody>
</table>

Additional notes:__________________________
### APPENDIX 2

**Statistical results**

**Table 12:** Statistical analysis of the size of the lesions in relation to the location (mandible vs. maxilla).

<table>
<thead>
<tr>
<th></th>
<th>Mandibular lesions</th>
<th>Maxillary lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Size (cm)</td>
<td>5.11</td>
<td>3.81</td>
</tr>
<tr>
<td>SD</td>
<td>4.11</td>
<td>1.97</td>
</tr>
<tr>
<td>SEM</td>
<td>0.6</td>
<td>0.49</td>
</tr>
<tr>
<td>Total number</td>
<td>47</td>
<td>16</td>
</tr>
<tr>
<td>P-value</td>
<td>0.2321</td>
<td></td>
</tr>
<tr>
<td>95% conf. interv.</td>
<td>-0.85 to 3.44</td>
<td></td>
</tr>
</tbody>
</table>

**Table 13:** Statistical analysis of the difference between the size of the lesions in Juvenile OF and OF.

<table>
<thead>
<tr>
<th></th>
<th>Size JOF</th>
<th>Size OF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>8.14</td>
<td>4.36</td>
</tr>
<tr>
<td>SD</td>
<td>3.58</td>
<td>3.54</td>
</tr>
<tr>
<td>SEM</td>
<td>1.35</td>
<td>0.47</td>
</tr>
<tr>
<td>N</td>
<td>7</td>
<td>56</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0099</td>
<td></td>
</tr>
<tr>
<td>95% conf. interv.</td>
<td>0.94 to 6.63</td>
<td></td>
</tr>
</tbody>
</table>