Odontogenic Tumours: A 10 year retrospective study in South African teaching hospital

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Dentistry in the branch of Oral pathology.

Johannesburg, 2018

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DECLARATION

I, Mpatikana Leslie Galane declare that this research report is my own, unaided work. It is being submitted for the Master of Science at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

.....

(Signature of candidate)

3rd day of July 2018 in Parktown

DEDICATION

This piece of work is dedicated to my late grandfather (Mr. Mathotile Andries Galane), what a hardworking man, a multitalented and very smart someone. Who saw the worthiness of education and encouraged me timeously to invest in it.

And

To my late friend, a brother to me (Mr. Amogelang Makgae), Amo. You took your illness with courage and tenacity. Unfortunately men proposes, but God disposes.

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to my supervisor and the Head of Department of Oral Pathology Dr Sizakele Ngwenya for her patience, boundless advice and constructive comments at every stage of this research project. Your extreme sacrifices and continuous guidance towards this research project are greatly valued.

I sincerely extend my thanks to the former Chief Executive Officer / Head of School: Wits School of Oral Health Sciences (Prof. Phumzile Hlongwa) and also to the current Chief Executive Officer / Head of School: Wits School of Oral Health Sciences (Prof. Simon Nemutandani) for granting us the permission to conduct this research project because if it were not for you, this research project wouldn't have been a success.

To my grandmother, Mrs Elizabeth Galane, my parents, Mrs Martha and Mr Johannes Galane thanks for showing me the greatest love of all times and the support you gave me through my continuous studies is immeasurable.

To my greatest pillar of strength my aunt (Rakgadi Maria waga Selamolela) her continuous and valuable emotional support and encouragement at every moment in my life.

Mr Moeketsi Montsho, Miss Lindiwe and Cynthia Galane for their immeasurable encouragement at every single stage of this research report. I believe I am an excellent role model that you proud yourself with continuously.

To my nieces and nephews (Johannes, Kwena, Ofentse, Phenyo, Mmaletjema and Malaika) you always excite me and rejuvenate my strength when research has despondent me.

To Elias Malunda Msiza, Ngoako Jay Morokolo and Donald Makhafola for their valuable inputs, supports and creative assistance during the analysis and compilation of the data in this research project.

To my friends and colleagues Drs Nare Chokoe and Sibongile Mahlangu for their resourceful assistance, support and guidance through this tireless work of research.

ABSTRACT

Background:

Odontogenic tumours (OTs) comprise a group of hamartomas, benign and malignant neoplasms arising from odontogenic epithelium entrapped within the jaws or in adjacent soft tissues. The first attempt by the World Health Organisation (WHO) to classify OTs was based on the epithelial mesenchymal interactions in these tumours. This was followed by three revisions in 1992, 2005 and 2017 following developments in immunohistochemistry and molecular biology techniques. One of the main modifications in the 2005 classification was the inclusion of odontogenic keratocyst (OKC) as a keratocystic odontogenic tumour (KCOT), due to its local aggressive behaviour and recurrence rate. Takata and Slootweg (2017) concluded that KCOT and calcifying cystic odontogenic tumour (CCOT) behave clinically as non-neoplastic lesions, and should therefore be classified as cysts. In the WHO classification (2017), KCOT and CCOT have been reclassified as OKC and calcifying odontogenic cyst (COC), respectively, until evidence that is more tangible suggests otherwise. Cemento-ossifying fibroma (COF) which occurs in the tooth-bearing areas of the jaws is engraved as a benign mesenchymal OT in the 2017 WHO classification, as it is believed to be of odontogenic origin.

The aim of the study:

The aim of the study was to determine the prevalence of OTs in the Department of Oral Pathology at the Wits Oral Health Centre from 2004 to 2013.

Patients and Methods:

The histopathology records of 392 patients diagnosed with OTs in the Department of Oral Pathology, Wits School of Oral Health Sciences, during a 10-year period were reviewed and reclassified according to the 2017 WHO classification of OTs. Clinical data including age, gender and anatomical distribution of lesions was collected and analysed. The data was captured into a Microsoft Excel spreadsheet. After cleaning, the data was imported into Stata IC/14 software for analysis. Descriptive statistics were reported for the purposes of this investigation. Continuous data (age) was analysed using parametric analysis methods and presented as mean (standard deviation) or median (minimum-

maximum). Frequency tables were plotted and clinico-pathological features (age, gender, race, diagnosis and site of involvement) were reported in the form of numbers and percentages. Proportions, histograms and pie charts were used to summarise these results.

Results: OTs accounted for 2.87% of all oral and maxillofacial lesions (n = 13665). There were 385(98.2%) benign OTs and 7 (1.8%) malignant OTs, the latter comprised 6 carcinomas and 1 sarcoma. The 3 most common OTs in descending order of frequency were ameloblastoma (AMB) 256 (62%), cemento-ossifying fibroma (COF) 44 (11.22%) and odontogenic myxoma (OM) 29(7.40%).

OTs with odontogenic epithelium in a mature fibrous stroma without odontogenic ectomesenchyme contributed 71.95% towards all the benign OTs, which attributed this group of lesions to be the most common group within all the benign OTs. AMB was the most common (92.42%) OT followed by AOT (7.58%) within OTs with odontogenic epithelium in a mature fibrous stroma without odontogenic ectomesenchyme.

The mean age of patients diagnosed with OTs was 30.88 years. The mean age of patients diagnosed with conventional AMB was 33.81 years, standard deviation 15.52 years with a range of 6 to 81 years. Of all the OTs, 122 (31.12%) occurred in the first three decades of life, with a peak incidence in the second decade, 91 (23.21%). The mean age of patients with benign OTs was 27.31 years whereas the mean age for patients with malignant OTs was 47 years. The male to female ratios for benign and malignant OTs were 1: 1.1 and 1:0.8 respectively. Both benign and malignant OTs showed a predilection for the posterior region of the mandible.

Conclusions: AMB was the most commonly seen odontogenic tumour. This finding is similar to those from Asian and African series. The variations observed between this study and those series are largely attributed to the 2017 WHO reclassification of OTs.

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- World Health Organisation-WHO
- South Africa-SA
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- Sclerosing odontogenic carcinoma –SOC
- Standard Deviation - STDV

CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

The literature review in this chapter will highlight findings of previous studies in order to set a solid foundation of the study as well as to inform the current study of the systematic developments of related studies on OTs**.** The literature review revolves around the prevalence of OTs, types of OTs, relative frequency of OTs and site of involvement. Furthermore, this chapter provides the problem statement, which explains why the study was executed. This is followed by a section which outlines the aim as well as the objectives of the study.

1.1 INTRODUCTION

Odontogenesis is a process that involves the interaction between ectodermal and ectomesenchymal tissues. The mandible and maxilla are rich with remnants of these tissues and may give rise to a heterogeneous group of odontogenic lesions (Melrose, 1999). OTs comprise a group of hamartomas, benign and malignant neoplasms arising from odontogenic epithelium entrapped within the jaws or in adjacent soft tissues (Philipsen et al., 2005; Regezi et al., 2008; Neville et al., 2009; Mamabolo et al., 2011).

The first attempt by the World Health Organisation (WHO) to classify OTs was based on the epithelial mesenchymal interactions in OTs (Pindborg and Kramer, 1971). Owing to developments in immunohistochemistry and molecular biology techniques, the WHO classification of OTs has been reviewed thrice in 1992 (Kramer et al., 1992), 2005 (Barnes et al., 2005) and 2017 (El-Naggar et al., 2017).

One of the main modifications in the 2005 classification was the inclusion of the odontogenic keratocyst (OKC). Due to its local aggressive behaviour and tendency to recur, the OKC was reclassified as the keratocystic odontogenic tumour (KCOT) (Pogrel, 2004; da-Costa et al., 2012). In the WHO classification (2017) KCOT and calcifying cystic odontogenic tumour (CCOT) have been reclassified as OKC and calcifying

odontogenic cyst (COC) respectively due to inadequate concrete evidence to support their classification as OTs in 2005 (El-Naggar et al., 2017). Takata and Slootweg (2017) reaffirmed the change citing the non-neoplastic clinical behavior of these lesions (El-Naggar et al., 2017). They further emphasised the need to differentiate between neoplastic and non-neoplastic cystic lesions. Cemento-ossifying fibroma (COF) presenting in the tooth-bearing areas of the jaws has been included in the list of benign mesenchymal OTs in the 2017 WHO classification, as it is believed to be of odontogenic origin (El-Naggar et al., 2017).

OTs may exclusively involve gingiva (peripheral type) or the jawbones (central type). Central OTs are often asymptomatic, diagnosed in a late expansile stage and require wide excision with devastating consequences for dental development and jaw growth in children (Mamabolo et al., 2011). According to the 2017 WHO classification, OTs are grouped into two categories, benign and malignant. Furthermore, the benign group is sub-divided into three more sub-categories depending on whether they are derived from odontogenic epithelium, ectomesenchyme or both; the malignant OTs are divided into three categories carcinoma, carcinosarcoma or sarcoma (El-Naggar et al., 2017) .

1.2 LITERATURE REVIEW

1.2.1 General Epidemiology of OTS

The overall and relative frequency of individual OTs differs from region to region (Barnes et al., 2005). Racial groupings, genetic make-up, terminology and the WHO classifications used are thought to be factors contributing to the geographic variation in the frequency of OTs (Ochsenius et al., 2002). The variation in the frequency of OTs is a common feature from different studies in different parts of the world. Some authors have reported that OTs are rare with a relative frequency of 1% (Ochsenius et al., 2002); while others have reported an OT prevalence of 32% (Adebayo et al., 2005). Malignant neoplasms are comparatively rare and comprise 1% of all jaw tumours (Regezi and Sciubba, 1993; Ochsenius et al., 2002; Saghravanian et al., 2010).

OTs demonstrate a female predilection (Arotiba et al., 1997; Santos et al., 2001; Ochsenius et al., 2002; Tawfik and Zyada, 2010) whereas other studies (Adebayo et al., 2002; Ladeinde et al., 2005; Avelar et al.,2008; Luo and Li 2009; Siriwardena et al., 2012) have reported that the mandible is the most common primary site for OTs, especially in the posterior region (molar area) for a significant number of OTs, most notably ameloblastoma (AMB) (Odukoya,1995; Ladeinde et al., 2005;) and KCOT(Dunfee et al., 2006; Servato et al., 2013).

Non-African studies particularly those conducted in Europe and America (Mosqueda-Taylor et al., 1997; Ochsenius et al., 2002; Buchner et al., 2006) generally report odontomas (ODTs) as the most common OTs while those from Africa (Adebayo et al., 2002; Ajayi et al., 2004; Adebayo et al., 2005; Simon et al., 2005; Tawfik and Zyada 2010; Lawal et al., 2013) report AMBs as the most common. ODTs are asymptomatic and are only detected during routine dental checkup. Lack of adequate healthcare facilities, skills shortage and cultural beliefs have contributed to the regional difference in the relative frequency of OTs (Ochsenius et al., 2002; Adebayo et al., 2005; Ladeinde et al., 2005).

In studies conducted by researchers in various geographical areas such as Sri Lanka, Brazil, China and Africa using the 2005 WHO classification of OTs, the most frequent OTs were AMB, KCOT and ODTs (Jing et al., 2007; Luo and Li, 2009; Tawfik and Zyada, 2010; Osterne et al., 2011; Siriwardena et al., 2012). In studies that utilized the 1992 classification, the sequence of the most frequent OTs was AMB, odontogenic myxoma (OM) for African or ODTs for non-African populations respectively (Arotiba et al.,1997; Santos et al., 2001;Adebayo et al., 2005; Simon et al., 2005).

1.2.2 Benign OTs

Ameloblastoma (AMB)

Some entities classified as benign OT are of a hamartomatous nature such as ODTs, whereas others are locally aggressive, as is the case with AMB. AMB is the most common tumour followed by KCOT and ODTs (Jing et al., 2007; Osterne et al., 2011; Siriwardena et al., 2012; Sekerci et al., 2014). With the inclusion of KCOT into the 2005 WHO classification of OTs, the frequency of AMB in comparison to other OTs has decreased significantly (Siriwardena et al., 2012).

According to the 2005 classification of OTs, the three variants of AMB are solid/multicystic, unicystic, or peripheral/ extraosseous lesions (Carlson et al., 2006; Neville et al., 2009). In the 2017 WHO classification the solid/multicystic ameloblastoma has been renamed the conventional ameloblastoma, and the metastasizing ameloblastoma has been moved to the benign category due to similar histological features with benign ameloblastomas (EL-Naggar et al., 2017).

The classification of desmoplastic ameloblastoma (DA) is a subject of controversy with some authors regarding it as a histological variant of solid/multicystic AMB, while others consider it to be a separate clinicopathological entity largely due to its specific clinical, radiological, and histological features (Barnes et al., 2005). In the 2017 WHO classification of OTs, DA was reclassified as a histological variant of the conventional AMB (EL-Naggar et al., 2017), as opposed to the distinct clinicopathological entity it was described to be in the 2005 classification.

Studies from Brazil (da Costa et al., 2012; Servato et al., 2013), Egypt (Tawfik and Zyada, 2010, and China (Luo and Li 2009) based their case series on the 2005 WHO classification. Contrary to reports by Lawal et al., 2013, Siriwardena et al., 2012, Luo and Li, 2009, Tawfik and Zyada, 2010 and Servato et al., 2013, the authors did not specify the four variants of AMB. These inconsistencies complicate the analysis and

comparison of the relative frequencies of the AMB variants globally and in sub-Saharan Africa.

Several reports have discussed the geographic variation in the prevalence of OTs, and in particular AMB and ODTs. Some studies have suggested that AMBs are more common in Asians and Africans than in Caucasians (Sekerci et al., 2014).The age range and gender distribution of AMB varies widely. AMB is the only benign OT common in patients over the age of 80 years (Reichart et al., 1995). Sekerci et al. (2014) reported an age range from 10 to 84 years in their case series. Several reports highlighted 34.2 years as the mean age for AMB (Siriwardena et al., 2012; Jing et al., 2007; Osterne et al., 2011; Ladeinde et al., 2005).

The variation in the gender distribution of AMB has been reported in several studies (Dhanuthai, 2004; Ogunsalu, 2003; Siriwardena et al., 2012). AMB occurred almost equally between the genders, while studies from Nigeria, Egypt, Iran and India showed a male predominance (Gupta et al., 2010; Saghravanian et al., 2010; Tawfik and Zyada, 2010; Adebayo et al., 2002). In Turkey, AMB showed a female predominance (Olgac et al., 2005). Peripheral and desmoplastic variants of AMB tend to occur more frequently in older patients (Siriwardena et al., 2012).

Regarding the site of occurrence, AMB showed a strong predilection for the mandible with less than 10% presenting in the maxilla (Arotiba et al., 1997; Tawfik and Zyada, 2010; da costa et al., 2012; Lawal et al., 2013). The mandibular molar and ramus regions are commonly associated with AMB (Arotiba et al., 1997; Ladeinde et al., 2005; Sriram and Shetty, 2008; Mamabolo et al., 2011; Tawfik and Zyada, 2010; Skereci et al., 2014). Reichart et al. (1995) reported that AMBs involving the anterior region are more commonly seen in Africans..

Keratocystic odontogenic tumour (KCOT)/ Odontogenic keratocyst (OKC)

KCOT is an intraosseous cystic neoplasm characterised by a lining of parakeratinised variants stratified squamous epithelium and its uniqueness in its histopathology

warranted it to be differentiated from other keratin-producing cysts (Barnes et al., 2005).. KCOT together with OM, adenomatoid odontogenic tumour (AOT) and ODTs have been reported to be the second most frequent OTs in different studies globally (Arotiba et al., 1997; Santos et al., 2001; Ajay et al., 2004; Adebayo et al., 2005; Simon et al., 2005; Luo and Li, 2009). The variable relative frequencies differ from region to region because of genetic and /or external factors. Inclusion of the KCOT in the 2005 WHO classification of OTs produced a significant increase in the prevalence of OTs prior to the 2017 WHO classification (Gaita ‘n Cepeda et al., 2010).

According to da-Costa et al. (2012) the KCOT was the most common tumour in males followed by AMB and ODTs. A finding that mirrors those of previous studies that have examined the prevalence of OTs (Luo and Li, 2009; Tawfik and Zyada, 2010) have confirmed this finding. However, Osterne et al. (2011) reported a female predilection in KCOT, followed by AMB and ODTs. The age range for the neoplasm is 8-68 years (Osterne et al., 2011) with a bimodal peak in the second and third decades of life (Lawal et al., 2013). The KCOT has a marked predilection for the mandible (Gupta et al., 2010; Tawfik and Zyada, 2010; Lawal et al., 2013). However, Servato et al. (2013) reported six cases of KCOT that occurred in the posterior maxilla. The clinical features for KCOT include a potential for local destruction and a tendency for multiplicity, particularly when the lesion is associated with nevoid basal cell carcinoma syndrome (Madras and Lapointe, 2008).

Odontomas (ODTs)

ODTs are considered tumour-like malformations or hamartomas of dental tissue rather than true odontogenic neoplasms (Jing et al., 2007). They are categorised as OTs of mixed odontogenic epithelial and odontogenic ectomesechymal origin (Barnes et al., 2005). As of 2017, ameloblastic fibrodentinoma and ameloblastic fibro-odontoma have been classified as types of ODTs in addition to complex and compound OTs. American studies show that ODTs are the commonest OTs in Mexico and Chile (Mosqueda-Taylor et al., 1997; Ochsenius et al., 2002). OTs are more frequently encountered in females

(Avelar et al., 2008; Saghravanian et al., 2010; Osterne et al., 2011).

Other published series of OTs reported no gender predilection (Buchner et al., 2006) or a slight predilection for male patients (Fernandes et al., 2005). In general, ODTs are the most common lesions in the maxilla (Servato et al., 2013). Moreover, complex and compound ODTs have a predilection for the anterior mandible and the anterior maxilla respectively (Avelar et al., 2008; Lawal et al., 2013). Several studies have reported similar clinicoradiologicopathological features and relative frequencies on ODTs (Mosqueda-Taylor et al., 1997; Fernandes et al., 2005; Ladeinde et al., 2005; Buchner et al., 2006; Tawfik and Zyada, 2010).

Adenomatoid odontogenic tumour (AOT)

The AOT is a benign, slow but progressively growing OT (Barnes et al., 2005) composed of odontogenic epithelium arranged in variable histological patterns; the epithelium is embedded in mature connective tissue stroma. In the 1992 WHO classification of OTs, the AOT was classified as a tumour of mixed odontogenic epithelium and odontogenic ectomesenchyme origin. (Kramer et al., 1992). However, since 2005, the AOT is classified as a benign epithelial OT (Barnes et al., 2005).

The AOT is considered to be the fourth or fifth most common OT with a relative frequency of 2-39% of all OTs (Philipsen et al., 1999; Philipsen et al., 1991; Philipsen et al., 2007). Saghravanian et al. (2010) reported the AOT as the third most common OT among patients in Iran. This finding is inconsistent with studies from Africa (Arotiba et al., 1997; Ladeinde et al., 2005; Adebayo et al., 2005).

The AOT occurs in a relatively younger age group (Santos et al., 2001; Tawfik and Zyada, 2010). The age range for AOT is between 1 to 38 years (Adebayo et al., 2005; Siriwardena et al., 2012). Several studies documented a female predilection (Mosqueda-Taylor et al., 1997; Fernandes et al., 2005; Tawfik and Zyada, 2010; Saghravanian et al., 2010). Ochsenius et al. (2002) reported a predilection for the anterior maxilla (Sriram and Shetty, 2008; Siriwardena et al., 2012). An uncommon presentation of AOTs, in the

posterior mandible has been reported. (Mosqueda-Taylor et al., 1997; Adebayo et al., 2004; Ladeinde et al., 2005). Siriwardena et al., 2012 reported a unilocular radiolucency extending from the premolar to molar region.

Odontogenic myxoma / myxofibroma (OM)

Odontogenic Myxoma (OM) is a non-encapsulated, infiltrative benign OT of ectomesenchymal origin. Several studies (Adebayo et al., 2004; Ladeinde et al., 2005) in Africa used the 1992 WHO classification of OTs and reported OM as the second most common OT, however a study in Turkey (Olgac et al., 2005) had a dissimilar finding. The majority of OMs present between the second and fourth decades of life with a peak incidence in the third decade (Muzio et al., 1996; Simon et al., 2004). Arotiba et al. (1997) and Lu et al. (1998) reported an equal gender predilection for OM, but other studies have reported a female predilection (Mosqueda-Taylor et al., 1997; Ochsenius et al., 2002; Ladeinde et al., 2005; Saghravanian et al., 2010; Osterne et al., 2011).

Most OM present in the mandible (Odukoya, 1995; Simon et al., 2004; Ladeinde et al., 2005). Several authors (Ochsenius et al., 2002; Adebayo et al., 2005) have reported a maxillary predilection of OM.

The other OTs, such as squamous odontogenic tumour (SOT), calcifying epithelial odontogenic tumour (CEOT), ameloblastic fibroma (AMBF), ameloblastic fibrodentinoma (AMBFD), ameloblastic fibro-odontoma(AMBFO), cementoblastoma (CB), odontoameloblastoma, calcifying cystic odontogenic tumour/ calcifying odontogenic cyst(COC/ CCOT) and dentinogenic ghost cell tumour (DGCT) comprised less than 5% of several OT series globally (Jing et al., 2007; Avelar et al., 2008; Siriwardena et al., 2012; Servato et al., 2013; Sekerci et al., 2014).

In Turkey Sekerci et al., 2014 reported a prevalence of 11.01% for CEOTs. The OAMB is an extremely rare benign odontogenic tumour with limited literature available. Together, Jing et al. (2007) and Saghravanian et al. (2010) reported three OAMBs in their case

series respectively. In Brazil Avelar et al. (2008) reported a relative frequency of 6.3% for CCOT.

Tumours originating from odontogenic epithelium with odontogenic ectomesenchyme were the least common benign OTs in Nigeria, Lawal et al. (2013). The most common odontogenic ectomesenchymal tumours were AMBF, AMBFO and CCOT.

Cemento-ossifying fibroma (COF)

The COF is a new addition to the list of OTs of benign mesenchymal origin (EL-Naggar et al., 2017). COF is a rare benign fibro-osseous neoplasm affecting the maxillofacial bones (Cawson and Odell., 2008; Sridevi et al., 2016). It is most commonly seen in the third and fourth decades of life (Sanchis et al., 2004; Galdeano-Arenas et al., 2004). Females are affected several times more frequently than males (Cawson and Odell, 2008). The most common location is the mandible with 70-90% of all cases presenting at this site (Sanchis et al., 2004; Liu et al., 2010).

1.2.3 Malignant OTs

The advancement in diagnostic techniques necessitated a review of the 1992 WHO classification of malignant OTs (Eversole, 1999). The author defined ameloblastic carcinoma (AMCA) as a tumour that shows features of ameloblastic differentiation and exhibits cytological atypia. Malignant ameloblastomas (MAB) are characterised by ameloblastic differentiation and metastasis to distant sites despite not showing features of cytological atypia.

Although extremely rare with less than 100 cases reported globally, the highest frequency of malignant OT is surprisingly reported in African and Chinese populations (Ladeinde 2005, Jing et al., 2007; Luo and Li, 2009; Lawal et al., 2013). While studies from North and South America have conferred rates of 1.6% or lower (Daley and Wysocki, 1994; Fernandes et al., 2005; Buchner et al., 2006; Gaitan-cepeda et al., 2010). AMCA was reported as the only prevalent malignant OT (n=4; 1.6%) among

patients in the first two decades of life in a rural African population sample (Mamabolo et al., (2011).

In contrast, Lawal et al. (2013) reported a relative frequency of 1.1%, 2.6% and 0.4% for AMCA, primary intra-alveolar squamous cell carcinoma (PISCC), ameloblastic fibrosarcoma (AMFS) respectively. Luo and Li (2009) reported a relatively higher frequency (3.74%) for PISCC in comparison to other authors (Jing et al., 2007; Tawfik and Zyada 2010). In Sri Lanka, clear cell odontogenic carcinoma (CCOC) and PISCC were the common malignant OTs (Siriwarden et al., 2012).

Malignant OTs are rare; even more so in children (Arotiba 1996; Mosqueda-Taylor et al., 1997; Adebayo and Ajike 2002,). Servato et al. (2013) reported a higher average age for malignant OTs and suggested that they may be restricted to adults (Servato et al., 2013). Malignant OTs predominantly occur in patients older than 40 years (mean age: 64 years) (Lawal et al., 2013, Sekerci et al., 2014). Several authors (Sirram and Shetty, 2008; Luo and Li, 2009) reported a lower mean age of 46 years.

Most malignant OTs have a predisposition for the mandible (Jing et al., 2007; Avelar et al., 2008; Luo and Li, 2009; Tawfik and Zyada, 2010). However AMBCA, PISCC arising de novo and CCOC are commonly seen in the maxillary molar regions (Sekerci et al., 2014). Several authors (Ochsenius et al., 2002; Jing et al., 2007; Avelar et al., 2008) reported that most malignant OTs exhibited a male predilection with the exception of the CCOC and PIOC which presented more frequently in females (Sekerci et al., 2014). Lawal et al., (2013) reported malignant OTs to be relatively more common in Americans than Africans, the authors suggested this discrepancy may possibly be due to racial disparities and differences in genetic makeup.

1.3 RATIONALE FOR THE STUDY

Although a number of authors globally have re-evaluated OTs in alignment with the 2005 WHO classification of OTs (Jing et al., 2007; Avelar et al., 2008; Luo and Li, 2009; Tawfik and Zyada, 2010; Osterne et al., 2010; Da-Costa et al., 2012), the only study of a similar nature conducted in South Africa (SA) (Mamabolo et al., 2011), limited its

analysis to a paediatric population sample. This study seeks to evaluate the clinicopathological features and relative frequency of OTs in a South African population sample, and as far as we know, will be the first all-inclusive study evaluating OTs in our setting, since the reclassification of OTs in 2017. Knowledge gained in determining the prevalence of OTs will help formulate and inform policies relating to screening, early diagnosis and management of OTs in a South African context.

1.4 THE AIM OF THE STUDY

The aim of the study was to determine the prevalence of OTs in the Department of Oral Pathology at the Wits Oral Health Centre from 2004 to 2013.

1.5 THE OBJECTIVES FOR THE STUDY

The objectives were to:

- Determine the relative frequency of OTs seen in the Department of Oral Pathology at the Wits Oral Health Centre from 2004 to 2013.
- Classify OTs seen at Wits Oral Health Centre from 2004 to 2013 in alignment with the 2017 WHO classification of OTs and compare findings with those reported in literature.
- Determine the clinicopathological features of all OTs seen at the Department of Oral Pathology, Wits Oral Health Centre from 2004 to 2013.

CHAPTER 2:

RESEARCH METHODOLOGY

2.1 INTRODUCTION

This research project was implemented in multiple phases involving thorough planning and obtaining permission from various stakeholders before commencement of data collection. The phases included data collection and analysis, reporting of findings, shortcomings, conclusion and recommendations. This chapter focuses on the study design and setting, sample and sampling technique, inclusion and exclusion criteria, measuring tools and processes involved in data collection and analysis, and ethical considerations.

2.2 RESEARCH METHODS

2.2.1 The study design

This was a quantitative, retrospective, cross-sectional descriptive study conducted through record review.

2.2.2 Study setting

The Department of Oral Pathology, Wits School of Oral Health Sciences at the University of the Witwatersrand, Johannesburg is serviced by the Charlotte Maxeke National Health Laboratory Services in the City of Johannesburg, South Africa. The Department provides a microscopic diagnostic service to the Wits Oral Health Centre, Chris Hani Baragwanath Hospital, Charlotte Maxeke Academic Hospital and referral hospitals including Tembisa, Sebokeng, Leratong, Natalspruit hospitals and others.

2.2.3 Study population

All OTs as prescribed by the 2017 WHO classification of OTs diagnosed from January 2004 to December 2013 in the Department of Oral Pathology, Wits School of Oral Health sciences were included in the study.

2.2.4 Study sample

A convenient sample was selected.

2.2.5 Inclusion and Exclusion criteria

The inclusion criteria comprised all histologically confirmed OTs from both incisional and excisional biopsies diagnosed within the specified period (from January 2004 to December 2013).

Exclusion criteria: Histologically confirmed OTs with inadequate or missing data were excluded from this study.

2.3 DATA COLLECTION

2.3.1 Data collection

All OTs diagnosed from January 2004 to December 2013 were retrieved from the archives of the Department of Oral Pathology at the University of the Witwatersrand. As both incisional and excisional biopsies were included in the study, specimens were interpreted with caution to avoid duplication of the results.

Each case was independently re-evaluated by two oral pathologists and the diagnosis was adapted to the 2017 classification of OTs.

The Criteria (2017 Classification of OTs)

OTs were divided into 2 major groups based on 2017 WHO classification: benign (group 1) and malignant (group 2) groups.

The benign group is further subdivided into:

- Odontogenic epithelium without odontogenic ectomesenchyme.
- Odontogenic epithelium with odontogenic ectomesenchyme, with or without dental hard tissue formation.
- Odontogenic ectomesenchyme with or without included odontogenic epithelium.

The malignant group is further subdivided into:

1. Odontogenic carcinomas
2. Odontogenic carcinosarcoma
3. Odontogenic sarcomas

(El-Naggar et al., 2017)

Clinico-pathological features and demographic data (age, gender, race, diagnosis and site of involvement) were analysed and recorded in a data collection sheet (6.1 Annexure A).

Regarding site distribution, the maxilla was divided into 3 anatomic regions:

- Class 1: Anterior segment (distal aspect of the right canine to distal aspect of the left canine)
- Class 2: Posterior segment (mesial aspect of the first premolar distally).
- Class 3: lesions that extend into the anterior and posterior segments of the maxilla.

The mandible was divided into 4 anatomic regions: anterior, posterior and angle, ramus condyle:

- Class 1I : Anterior segment (distal aspect of the right canine to distal aspect of the left canine)
- Class 2: Posterior segment (mesial aspect of the first premolar to distal aspect of the third molar)
- Class 3: lesions from the distal aspect of the second molar to the condyle (Angle, ramus and condyle segments)
- Class4: lesions that extend into the anterior, posterior and ramus segments of the mandible

Any other site distribution not catered for in the list above was designated as other, with a provision to specify the exact site of the involvement.

2.3.2. Measurements, Data Collection and Data Analysis

Before the commencement of data collection, relevant permission and consent were sought to gain access to the research location. The data was captured into Microsoft Excel spread sheet. After cleaning the data, it was imported into Stata IC/14 software for analysis. Descriptive statistics were reported for the purposes of this investigation. Continuous data (age) was analysed using parametric analysis methods and presented as mean (standard deviation) or median (minimum-maximum). Frequency tables were plotted and clinico-pathological features (age, gender, race, diagnosis and site of involvement) were reported in the form of numbers and percentages. Proportions, histograms and pie charts were used to summarise these results.

2.4 ETHICAL CONSIDERATION

2.4.1 Permission to conduct study

In order to conduct this study, the researcher sought ethical clearance in writing from the Hospital Research and Ethics Committee (HREC) and from the Human Research Ethics Committee (Medical) of the Faculty of Health Sciences (HREC) at the University of the Witwatersrand. Approval was granted by the HREC and HREC (Medical) with reference

number: HREC/SEP 2015/03 (See 6.4 Annexure D) and M150828 respectively (See 6.5 Annexure E).

Formal approval to gain access to the study setting was also obtained from the Dean of Wits School of Oral Health Sciences and the Head of the Department of Oral pathology.

2.4.2 Confidentiality and anonymity assurance

Confidentiality and personal rights of the patients were ensured in this study by not using names or other identifiers. Each patient was allocated a case number and all patient identifiers were removed and kept on a separate link file accessible only to the researcher. All data extracted for the research was securely kept by the researcher and remained confidential.

CHAPTER 3

PRESENTATION OF RESULTS

In chapter 2, the research methodology in which the processes and tools of collecting data were thoroughly detailed. The focus of this chapter is on the data collected through a quantitative method described above on Odontogenic Tumours: A 10 year retrospective study in a South African teaching hospital. This section will be addressing the three main objectives of the study in depth.

3.1 Objective 1: The relative frequency of OTs seen at the Department of Oral Pathology, at the Wits Oral Health Centre from 2004 to 2013.

A total of 13665 oral and maxillofacial lesions, were seen and diagnosed between January 2004 and December 2013. Of these, 392 satisfied the criteria prescribed by the 2017 WHO classification of OTs for inclusion in the study. Three hundred and seventy two were intraosseous and twenty were peripheral OTs. The latter comprised peripheral AMB and 19 POF. There were 385(98.21%) benign OTs and seven (1.79%) malignant OTs (figure 3.1.1). Of the latter, six were carcinomas and one was a sarcoma.

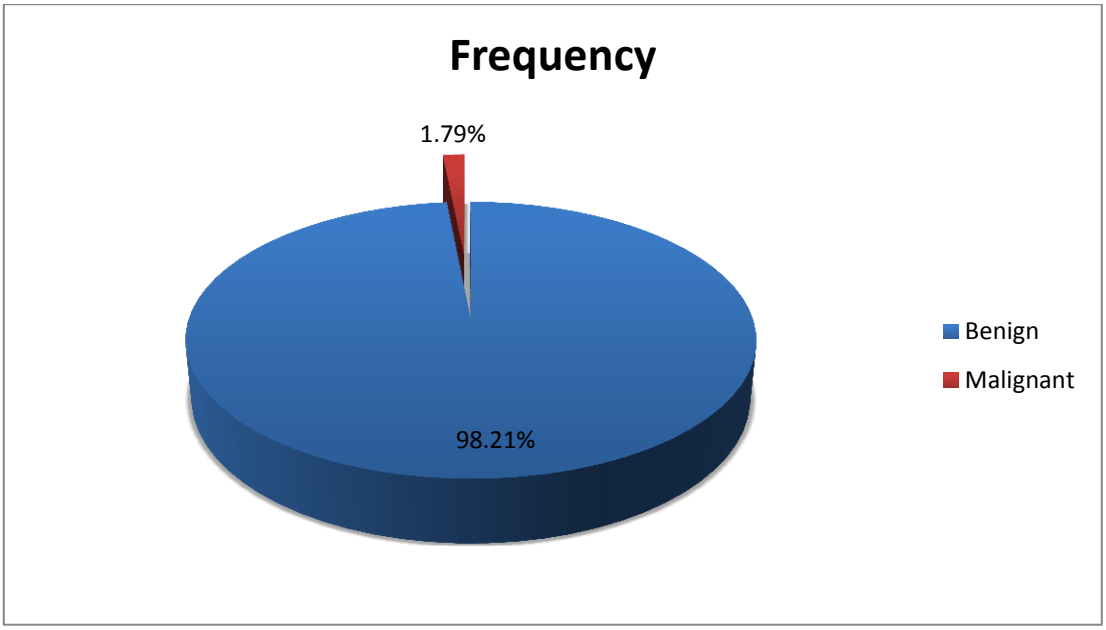

Figure 3.1.1 Benign and malignant tumour distribution

The three most common benign OTs in descending order of frequency were AMB 256 (66.5%), COF 44 (11.43%) and OM 29 (7.40%) (Table 3.1.1). The benign OTs comprised 277 (71.92%) epithelial, 14 (3.64%) mixed epithelial-mesenchymal, and 94 (24, 42%) mesenchymal tumours. AMB (92, 42%), COF (46, 8%) and POF (20, 21%) were the most common benign epithelial, epithelial-mesenchymal and mesenchymal OTs. The distribution of various OTs is presented in Table 3.1.1.

Table 3.1.1 Distribution of benign odontogenic tumours

BENIGN ODONTOGENIC TUMOURS				
Epithelial Odontogenic Tumours (EOT)				
Tumours	**Frequency (n)**	**Percentage (% of EOT)**	**Percentage (% of benign OT)**	**Percentage (% of all tumours)**
Ameloblastoma (total)	256	92.42	66.5	65.30
Conventional Ameloblastoma	202	72.92	52.47	51.53
Unicystic Ameloblastoma(total)	40	14.44	10.39	10.20
Ameloblastoma unicystic type 1	13	4.69	3.38	3.31
Ameloblastoma	4	1.44	1.04	1.02

unicystic type 2 Ameloblastoma unicystic type 3 Unicystic ameloblstoma(unclassified)	21 2	7.58 0.72	5.45 0.52	5.35 0.51
Ameloblastoma(unclassified)	13	4.69	3.38	3.32
Peripheral ameloblastoma	1	0.36	0.26	0.26
Adenomatoid odontogenic tumour	21	7.58	5.45	5.36
Epithelial Odontogenic Tumours(Total)	**277**	**100**	**71.94**	**70.12**
Mixed Epithelial and Mesenchymal Odontogenic Tumours (MEMOT)				
Percentage(% of MEMOT)				
Odontomas(total)	14		3.64	3.57
Complex odontoma Compound odontoma Ameloblastic fibro-odontoma	12 1 1	85.71 7.14 7.14	3.12 0.26 0.26	3.06 0.26 0.26
Mixed Epithelial And Mesenchymal Odontogenic Tumours (Total)	**14**	**100**	**3.64**	**3.57**
Mesenchymal Odontogenic Tumours (MOT)				
Percentage(% of MOT)				
Cemento-ossifying fibroma	44	46.81	11.43	11.22
Odontogenic myxoma/myxofibroma	29	30.85	7.53	7.40
Odontogenic fibroma(total)	20	21.28	5.19	5.10
Peripheral Odontogenic Fibroma(total)	19	20.21	4.93	4.84
Epithelium poor	9	9.57	2.34	2.30

Epithelium rich Unspecified	8 2	8.51 2.13	2.07 0.52	2.04 0.51
Odontogenic fibroma	1	1.06	0.26	0.26
Cementoblastoma	1	1.06	0.26	0.26
Mesenchymal Odontogenic Tumours (Total)	**94**	**100**	**24.42**	**23.98**
BENIGN TUMOURS(TOTAL)	**385**	**-**	**100**	**98.21**

Table 3.1.2 Distribution of malignant odontogenic tumours

Tumours	**Frequency (n)**	**Percentage (% of malignant OT)**	**Percentage (% of all OT)**
MALIGNANT ODONTOGENIC TUMOURS			
Carcinomas			
Ameloblastic carcinoma	4	57.14	1.02
Clear cell odontogenic carcinoma	1	14.29	0.26
Sclerosing odontogenic carcinoma	1	14.29	0.26
Carcinomas(total)	**6**	**85.71**	**1.53**
Sarcomas			
Ameloblastic fibrosarcoma	1	14.29	0.26
Sarcomas(total)	**1**	**14.29**	**0.26**
MALIGNANT TUMOURS(TOTAL)	**7**	**100**	**1.79**

3.2 Objective 2: OTs seen at the Wits Oral Health Centre from 2004 to 2013 in alignment with the 2017 WHO classification of OTs and compare findings with those reported in literature.

The most common tumour in the subcategory of benign tumours originating from odontogenic epithelium without odontogenic ectomesenchyme was AMB 256(62%). Of these 202, 40 and one were classified as conventional, unicystic and peripheral AMB respectively. Type 3 unicystic AMB was the most common and represented 52, 5% of all unicystic AMB's. The remainder (n=13) of lesions diagnosed as AMB were not classified. AOT was the second most common tumour 21 (5.36%).

The most common tumour in the subcategory of benign tumours originating from odontogenic epithelium with odontogenic ectomesenchyme (with or without dental hard tissue) was complex ODT 12 (3.06%). Compound ODT and AMBFO represented 1 (0.26%) case each.

The most common tumour in the subcategory of benign tumours originating from odontogenic ectomesenchyme with or without odontogenic epithelium was COF 44 (11.22%). The second most common tumour in this subcategory was POF 20 (19%), nine (2.3%) of these were POF epithelium poor and eight (2.04%) POF epithelium rich. Conventional OF (0.26%) and CB (0.26%) represented one case each.

The most common malignant tumour in the subcategory of carcinomas was AMCA (n= 4; 1.02%). One CCOC (0.26%) and sclerosing odontogenic carcinoma (SOC) (0.26%) were reported. One ameloblastic fibrosarcoma (AMFS) (0.26%) represented the sarcoma subcategory of malignant odontogenic neoplasms. The distribution of various OTs is presented in Table 3.1.1.

3.3 Objective 3: The clinicopathological features of all OTs seen at the Department of Oral Pathology, Wits Oral Health Centre from 2004 to 2013.

The OTs in this series were encountered over a wide age range, from one to eighty two years. The mean age of patients was 30.88 years standard deviation 15.27 years. The mean age of patients with benign OTs was 27.31 years standard deviation 11.72 years whereas the mean age for patients with malignant OTs was 47 years standard deviation 24.54 years.

The mean age of patients diagnosed with conventional AMB was 33.81 years, Standard deviation 15.52 years with a range of 6 to 81 years. Whilst for AMBFO patients had the mean age of 16.5 years, standard deviation 2.12years with a range of 2 to 2 years. The mean age, standard deviation and age ranges of various OTs is presented in Table 3.3.1.

Table: 3.3.1 Mean age, standard deviations and age ranges of various odontogenic tumours

Tumours	Mean	SDTV	Min	Max
Benign: Odontogenic epithelium with ,mature, fibrous stroma without odontogenic ectomesenchyme				
Ameloblastoma conventional	33.81	15.52	6	81
Ameloblastoma unicystic type 1	23.38	11.32	10	46
Ameloblastoma unicystic type 2	21.25	8.42	13	29
Ameloblastoma unicystic type 3	19.90	8.44	8	37
Unspecified ameloblstoma	35.69	16.40	17	77
Unspecified unicystic ameloblstoma	20	8.49	14	26
Peripheral ameloblastoma	42	0	42	42
Adenomatoid odontogenic tumour	19.10	8.70	9	40
Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation				
Complex odontoma	23.83	12.00	9	50
compound odontoma	12	0	12	12
Ameloblastic fibro-odontoma	16.5	2.12	2	2

mesenchyme and or odontogenic ectomesenchyme with or without odontogenic epithelium				
Cemento Ossifying Fibroma	27.68	13.87	6	71
Odontogenic myxoma	27.79	11.531	1	63
Peripheral odontogenic fibroma poor	44.33	11	34	67
Peripheral odontogenic fibroma rich	35.63	16.53	15	57
Unspecified peripheral odontogenic fibroma	16	0	16	16
Odontogenic fibroma	2	0	67	67
Cementoblastoma	25	0	25	25
Malignant: Carcinoma				
Ameloblastic carcinoma	29.75	15.09	9	45
Clear cell odontogenic carcinoma	76	0	76	76
Sclerosing odontogenic carcinoma	44	0	44	44
: Sarcoma				
Ameloblastic fibrosarcoma	60	0	60	60
Total	**30.90**	**15.27**	**1**	**81**

Of all the OTs 122 (31.12%) occurred in patients in their first three decades of life, with a peak incidence in the second decade 91 (23.21%) (Figure 3.3.1). The age distribution in this series is presented in Table 3.3.2.

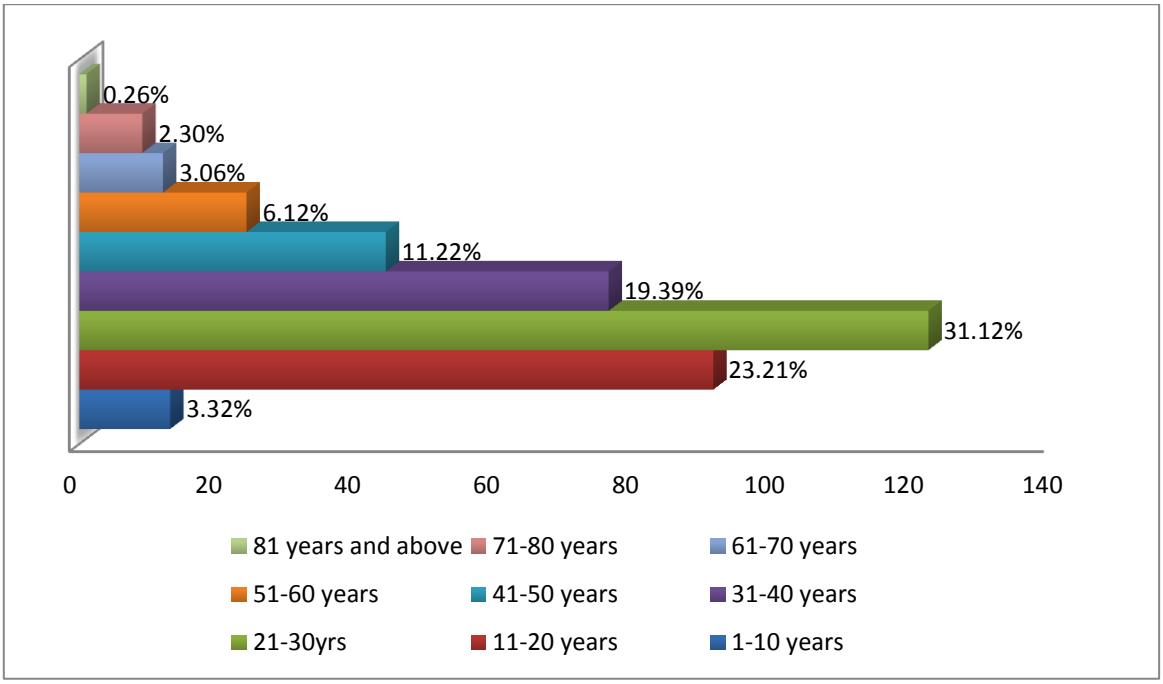

Figure: 3.3.1 Age group distribution of odontogenic tumours

Table: 3.3.2 Age group distribution of odontogenic tumours

.	Age (Years)									
	1-10	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81+**	**Total**
Benign: Odontogenic epithelium with ,mature, fibrous stroma without odontogenic ectomesenchyme										
Ameloblastoma in total	5	54	84	51	27	18	9	7	1	256
Conventional Ameloblastoma	1	35	67	43	23	17	9	6	1	202
Ameloblastoma unicystic type 1	1	4	6	0	2	0	0	0	0	13
Ameloblastoma unicystic type 2	0	2	2	0	0	0	0	0	0	4
Ameloblastoma unicystic type 3	3	9	6	3	0	0	0	0	0	21

Unspecified ameloblstoma	0	3	2	5	1	1	0	1	0	13
unicystic ameloblstoma (unspecified)	0	1	1	0	0	0	0	0	0	2
peripheral ameloblastoma	0	0	0	0	1	0	0	0	0	1
Adenomatoid odontogenic tumour	1	13	4	3	0	0	0	0	0	21
Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation										
Odontomas in total	3	5	4	0	2	0	0	0	0	14
Complex odontoma	2	4	4	0	2	0	0	0	0	12
compound odontoma	0	1	0	0	0	0	0	0	0	1
ameloblastic fibro-odontoma	1	0	0	0	0	0	0	0	0	1
Mesenchyme and or odontogenic ectomesenchyme with or without odontogenic epithelium										
Cemento Ossifying Fibroma	2	12	10	10	8	1	0	1	0	44
Odontogenic myxoma/myxofibroma	1	3	18	2	4	0	1	0	0	29
peripheral odontogenic fibroma in total	0	4	1	8	1	4	1	0	0	19
peripheral odontogenic fibroma epithelium poor	0	0	0	6	0	2	1	0	0	9
peripheral odontogenic fibroma epithelium rich	0	2	1	2	1	2	0	0	0	8
peripheral odontogenic fibroma (unspecified)	0	2	0	0	0	0	0	0	0	2
Odontogenic fibroma	0	0	0	0	0	0	1	0	0	1
cementoblastoma	0	0	1	0	0	0	0	0	0	1
Benign Tumours in Total	12	91	122	74	42	23	12	8	1	385
Malignant: Carcinoma										
Ameloblastic carcinoma	1	0	0	2	1	0	0	0	0	4
clear cell odontogenic carcinoma	0	0	0	0	0	0	0	1	0	1
seclrosing odontogenic	0	0	0	0	1	0	0	0	0	1

carcinoma										
Sarcoma										
Ameloblastic fibrosarcoma	0	0	0	0	0	1	0	0	0	1
Malignant Tumours in Total	1	0	0	2	2	1	0	1	0	7
Total	**13**	**91**	**122**	**76**	**44**	**24**	**12**	**9**	**1**	**392**

Of all OTs, 203 (51.79%) were encountered in women and 189 (48.21%) (Figure 3.3.1) were encountered in men, the male to female ratio was 1:1.1. AMB and AOT were more common in males than females with male to female ratios of 1: 0.8 and 1:0.8, respectively. Whereas complex ODTs, COF, OM and POF in total had a predilection for females, with male to female ratios of 1:3,1:2.1,1:2.2 and 1:2.5, respectively.

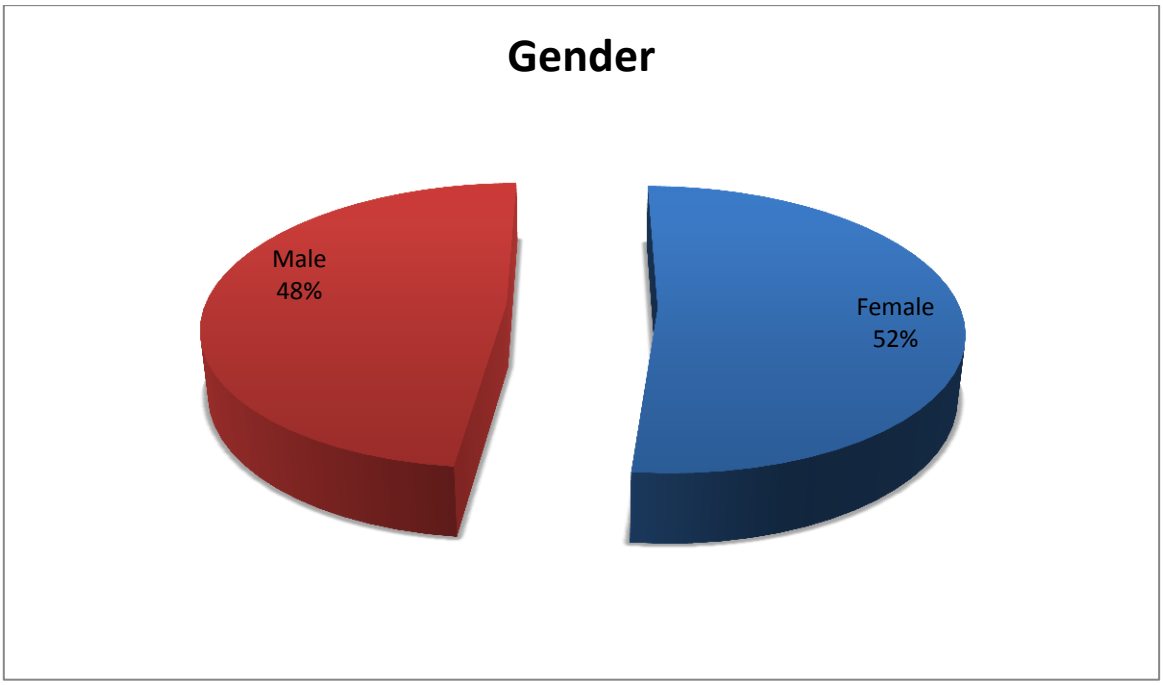

Figure: 3.3.2: Gender distribution of odontogenic tumours

Among malignant OTs, four were encountered in men and three occurred in women, with a male to female ratio of 1:0.8. The gender distribution of OTs is presented in Table 3.3.3.

Table: 3.3.3: Gender distribution of odontogenic tumours.

Tumours	Male	Female	Total	Male to female ratio
Odontogenic epithelium with ,mature, fibrous stroma without odontogenic ectomesenchyme				
Ameloblastoma in total	140	116	256	1:0.8
Conventional Ameloblastoma	113	89	202	1:0.7
Ameloblastoma unicystic type 1	3	10	13	1:3.3
Ameloblastoma unicystic type 2	2	2	4	1:1
Ameloblastoma unicystic type 3	14	7	21	1:0.5
Ameloblastoma(unclassified)	7	6	13	1:0.9
Unicystic ameloblstoma(unclassified)	1	1	2	1:1
Peripheral ameloblastoma	0	1	1	NA
Adenomatoid odontogenic tumour	12	9	21	1:0.8
Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation				

Odontoma	3	11	14	1:3.7
Complex odontoma	3	9	12	1:3
Compound odontoma	0	1	1	NA
Ameloblastic fibro-odontoma	0	1	1	NA
Mesenchyme and or odontogenic ectomesenchyme with or without odontogenic epithelium				
Cemento Ossifying Fibroma	14	30	44	1:2.1
Odontogenic myxoma/myxofibroma	9	20	29	1:2.2
eripheral odontogenic fibroma in total	5	14	19	1:2.5
peripheral odontogenic fibroma poor	1	8	9	1:8
peripheral odontogenic fibroma rich	3	5	8	1:1.7
unspecified peripheral odontogenic fibroma	1	1	2	1:1
Odontogenic fibroma	1	0	1	NA
cementoblastoma	1	0	1	NA
Benign Tumours in Total	185	200	385	1:1.1
Malignant:				
Carcinoma				
Ameloblastic carcinoma	2	2	4	1:1
clear cell odontogenic carcinoma	0	1	1	NA
seclrosing odontogenic carcinoma	1	0	1	NA
Sarcoma				
Ameloblastic fibrosarcoma	1	0	1	NA
Malignant Tumours in Total	4	3	7	1:0.8
Total	**189**	**203**	**392**	**1:1.1**

Benign OTs were more common in the mandible 316 (80.61%) than maxilla 68(17.4%) (Figure 3.3.3), with a maxilla to mandible ratio of 1:2.5 (table 3.3.4) and only eight OTs occurred at special sites.

Overall, both benign and malignant OTs showed a predilection for the mandible, especially the posterior region. AMB, complex ODTs, COF, OM and POF epithelium rich demonstrated a strong predilection for the mandible with maxilla to mandible ratios of 1:12.9, 1:2, 1:2.4, and 1:2.1 and1:7 respectively.

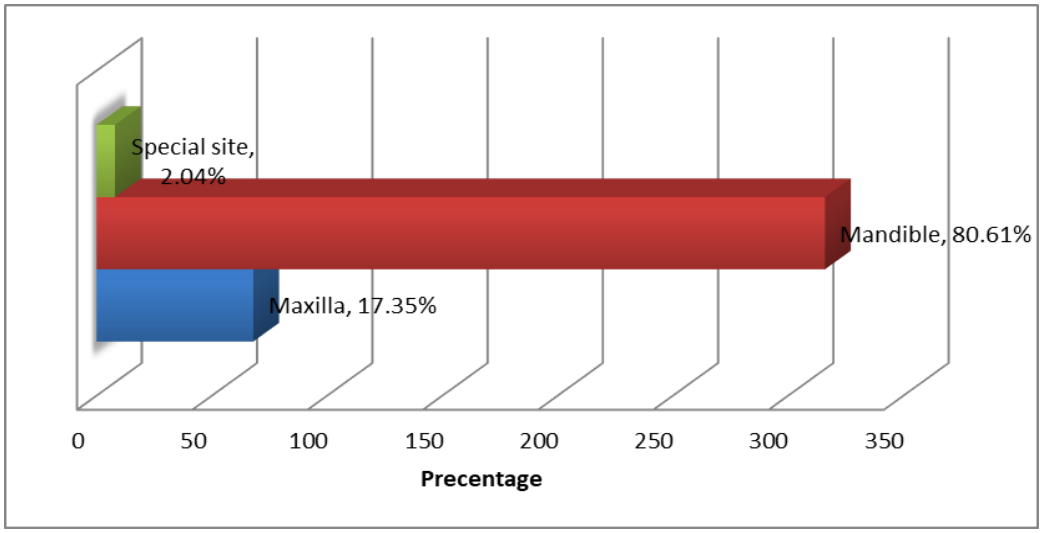

Figure: 3.3.3: Jaw distribution of odontogenic tumours

Of the four AMCA, three presented in the mandible and one in the maxilla. AOT and POF epithelium poor occurred in the maxilla more often than in the mandible. The anatomical distribution of each type of OT is summarised in Table 3.3.4.

Table: 3.3.4: Anatomical distributions of odontogenic tumours.

Tumours	Maxilla	Mandible	Other sites	Total	maxillary : mandibular ratio
Benign: Odontogenic epithelium with ,mature, fibrous stroma without odontogenic ectomesenchyme					
Ameloblastoma in total	18	232	6	256	1:12.9
Conventional Ameloblastoma	13	185	4	202	1:14.2
Ameloblastoma unicystic type 1	3	10	0	13	1:3.3
Ameloblastoma unicystic type 2	0	4	0	4	NA
Ameloblastoma unicystic type 3	1	20	0	21	1:20
Unspecified ameloblstoma	1	10	2	13	1:10
Unspecified unicystic ameloblstoma	0	2	0	2	NA
peripheral ameloblastoma	0	1	0	1	NA

Adenomatoid odontogenic tumour	13	8	0	21	1:0.6
Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation					
Odontomas in total	5	8	1	14	1:1.6
Complex odontoma	4	8	0	12	1:2
compound odontoma	1	0	0	1	NA
Ameloblastic fibro-odontoma	0	0	1	1	NA
mesenchyme and or odontogenic ectomesenchyme with or without odontogenic epithelium					
Cemento Ossifying Fibroma	13	31	0	44	1:2.4
Odontogenic myxoma	9	19	1	29	1:2.1
peripheral odontogenic fibroma in total	7	12	0	19	1:1.7
Peripheral odontogenic fibroma poor	6	3	0	9	1:0.5
Peripheral odontogenic fibroma rich	1	7	0	8	1:7
Unspecified peripheral odontogenic fibroma	0	2	0	2	NA
Odontogenic fibroma	1	0	0	1	NA
Cementoblastoma	0	1	0	1	NA
Benign Tumours in Total	59	299	8	366	1:5.1
Malignant: Carcinoma					
Ameloblastic carcinoma	1	3	0	4	1:3
clear cell odontogenic carcinoma	0	1	0	1	NA
seclrosing odontogenic carcinoma	1	0	0	1	NA
Sarcoma					
Ameloblastic fibrosarcoma	0	1	0	1	NA

Malignant Tumours in Total	2	5	0	7	1:2.5
Total	**68**	**316**	**8**	**392**	**1: 4.7**

Table: 3.3.5: Distribution of tumours by site of occurrence

Tumours	Maxila			Mandible				Other sites	Unknown	Total
	Class 1	Class 2	Class 3	Class 1	Class 2	Class 3	Class 4			
Benign: Odontogenic epithelium with ,mature, fibrous stroma without odontogenic ectomesenchyme										
Ameloblastoma in total	7	6	6	87	59	49	28	6	8	256
Conventional Ameloblastoma	5	5	4	73	44	35	27	4	5	202
Ameloblastoma unicystic type 1	0	1	1	6	2	3	0	0	0	13
Ameloblastoma unicystic type 2	0	0	0	0	2	2	0	0	0	4
Ameloblastoma unicystic type 3	1	0	0	3	8	5	1	0	3	21
Unspecified ameloblstoma	1	0	1	4	2	3	0	2	0	13
Unspecified unicystic ameloblstoma	0	0	0	1	0	1	0	0	0	2
peripheral ameloblastoma	0	0	0	0	1	0	0	0	0	1
Adenomatoid odontogenic tumour	6	2	4	4	2	0	0	0	3	21
Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation										
Odontoma in total	4	0	1	1	6	1	0	0	1	14
Complex odontoma	3	0	1	1	6	1	0	0	0	12
compound odontoma	1	0	0	0	0	0	0	0	0	1
ameloblastic fibro-odontoma	0	0	0	0	0	0	0	0	1	1
mesenchyme and or odontogenic ectomesenchyme with or without odontogenic epithelium										
Cemento Ossifying Fibroma	4	4	6	6	22	2	0	0	0	44
Odontogenic myxoma	3	4	2	9	6	2	1	1	1	29
Peripheral odontogenic fibroma in total	4	1	2	5	7	0	0	0	0	19
peripheral odontogenic fibroma poor	4	0	2	1	2	0	0	0	0	9
peripheral odontogenic fibroma rich	0	1	0	2	5	0	0	0	0	8
unspecified	0	0	0	2	0	0	0	0	0	2

peripheral odontogenic fibroma										
Odontogenic fibroma	1	0	0	0	0	0	0	0	0	1
cementoblastoma	0	0	0	0	1	0	0	0	0	1
Benign Tumours in Total	29	17	21	112	1036	54	29	7	13	385
Malignant: Carcinoma										
Ameloblastic carcinoma	0	0	0	1	0	2	0	0	1	4
clear cell odontogenic carcinoma	0	0	0	0	0	1	0	0	0	1
seclrosing odontogenic carcinoma	0	1	0	0	0	0	0	0	0	1
Sarcoma										
Ameloblastic fibrosarcoma	0	0	0	0	0	1	0	0	0	1
Malignant Tumours in Total	0	1	0	1	0	4	0	0	1	7
Total	**29**	**18**	**21**	**113**	**103**	**58**	**29**	**8**	**13**	**392**

Conventional AMB showed a strong predilection for the posterior mandible with thirteen AMBs presenting at that site and eight at nonspecified sites (Table 3.3.5) (1 on the right infra-orbital to lower border of right mandible, 1 on the left side of face, 1 on the left nasal mass extending from left maxillary sinus to nasal vestibules, 1 on the right side of the face,1 extending from the right nostril to the palate, 1 in the left maxillary sinus, 1 in the right maxillary sinus extending into the infraorbital fossa intra-osseosly, 1 right submandibular parotid and 1 extending into the cranium, sphenoid, orbit and nasal bones, maxilla and mandible posterior). AOT showed a strong predilection for the anterior maxilla (6) . The site of involvement was not specified in two AOTs.

Six of seven complex ODTs and twenty two of twenty four COFs involved the posterior mandible. Nine and one OMs occurred in the anterior mandible and the riight paranasal area(Table 3.3.5) respectively.Four epithelium poor POFs involved the anterior maxilla while five epithelium rich POFs which epresented in the posterior mandibular(Table 3.3.5).

Two AMCA occurred in the posterior mandible and one at site that was not specified. The anatomical distribution of each type of OT by site of occurrence is summarised in Table 3.3.5.

CHAPTER 4

DISCUSSIONS AND CONCLUSIONS

4.1 INTRODUCTION

This final chapter discusses results from chapter 3 and the discussions will be done in relation to the literature review. The study limitations will be included, and the conclusions drawn will be based on the findings. Recommendations emerging from the study's findings will form the latter part of the chapter.

4.2 The first objective for this study was to determine the relative frequency of OTs seen at the Department of Oral Pathology at Wits Oral Health Centre from 2004 to 2013.The discussion below forms part of this evolving objective.

The different OTs show variation in their biological and clinical behaviour. Information and knowledge relating to the population group at risk for developing various OTs, possible factors associated with the development of OT and relevant differential diagnoses can be identified through OT studies (Da Costa et al., 2012). Different classifications have been used to compare the relative frequencies of OTs and the exclusion and inclusion of recognised entities make it difficult to draw comparisons. Epidemiological OT studies in South Africa are extremely rare (Mamabolo et al., 2011). The literature search in sub-Saharan Africa revealed that such studies were mostly conducted in Nigeria (Arotiba et al., 1997; Adebayo et al., 2002; Adebayo et al., 2005; Ladeinde et al., 2005; Lawal et al., 2013; Anyanechi and Saheeb, 2014). Therefore, we aimed at investigating the prevalence of OTs in South Africa over a period of 10 years.

The Prevalence of OTs

In this study, OTs accounted for 2.87% of all oral and maxillofacial lesions, a figure lower than that reported in a study conducted in India (5.7%) (Ramachandra et al., 2014). Several epidemiological studies on OTs reported that the prevalence of OTs ranges from 1.2% to 15.5% (Buchner et al., 2006; Saghravanian et al., 2010; Varkhede et al., 2011; Taghavi et al., 2013; Alsheddi et al., 2015).

The exclusion of the KCOT and CCOT in the current classification (WHO 2017) may have been an important factor contributing to the lower prevalence of OTs in this study compared to previous research. Deepthi et al. (2016) cited racial difference as the most probable cause for the variation in the prevalence of OTs globally.

Malignant vs Benign

In this study, 98.21% of OTs were benign. This finding is slightly higher than reported in Nigeria (96.6% - 96.8 %) and Brazil (94.5%) (Anyanechi and Saheeb, 2014; Ladeinde et al., 2005; da Costa et al., 2012). Malignant OTs are extremely rare with reported incidences ranging from 0% to 6.1% (Santos et al., 2001; Lu et al., 1998). Malignant OTs comprised 1.77% of OTs. This finding is lower than those reported in Nigeria which reported 3.2% (Anyanechi and Saheeb, 2014) and 3.4% (Ladeinde et al., 2005). Malignant OTs are relatively more common in Americans than Africans (Lawal et al., 2013). The variation in the distribution of malignant OTs may be due to cultural variation and geographical settings among the different study populations (Kebede et al., 2017). Lawal et al. (2013) however, suggested the discrepancy may possibly be due to racial disparities and differences in genetic makeup.

Ameloblastoma (AMB)

The AMB was the most common OT in this study representing 65.3% of all OTs. These findings are comparable to those of two studies from Nigeria which reported 63% and 73% respectively. (Ladeinde et al., 2005; Adebayo et al., 2005). Reports from American (Daley et al., 1994; Ochsenius et al., 2002) and Indian (Ramachandra et al, 2014)

studies reported ODTs as the most common OTs followed by AMB. In this study, ODTs were the sixth most common OTs.

Keratocystic Odontogenic Tumours (KCOT) / Cemento-Ossifying Fibroma (COF)

The prevalence of OTs increased after the inclusion of OKC/KCOT in the classification of OTs in the 2005 WHO classification of OTs. However, the exclusion of the KCOT and CCOT in the WHO classification (2017) subsequent to their reclassification as odontogenic cysts (El-Naggar et al., 2017) may have led to the reduction in the prevalence of OTs, particularly in regions where KCOT was common; for instance in India, where KCOT has been reported as the second most common OT (Deepthi et al., 2016; Nalabolu et al., 2016). In this study, COF accounted for 11.22% of all OTs making it the second most common OT in this study. COF is a new addition to OTs, therefore the comparison of relative frequencies with previous studies on OTs is not possible.

Odontogenic Myxoma (OM)

In retrospective studies from Nigeria, Brazil and Mexico, OMs showed a relative frequency ranging from 6.5% to 17.7% (Mosqueda –Taylor et al., 1997; Ladeinde et al., 2005; Osterne et al., 2011). In this study OM comprised 7.40% of all OTs, slightly higher than results from previous studies (Nalabolu et al., 2016; Simon et al., 2005). Whilst both Kebede et al. (2017) and Ajayi et al. (2004) reported a prevalence rate of 8.36% for OM. In the current study OM was found to be the third most common OT. This result is consistent with the findings in reports from Nigeria (Ajayi et al., 2004) and Ethiopia (Kebede et al., 2017).

Adenomatoid Odontogenic Tumour (AOT)

The AOT comprised 5.36% of all OTs, a figure lower than reported in epidemiological studies in China (9%) (Jing et al., 2007) and India (7.89%) (Ramachandra et al., 2014). The current study's research findings are more comparable to the results (5.4 %) Avelar et al. (2008) reported in Brazil. Similar to findings by Varkhede et al. (2011) the AOT was

the fourth most common OT (5.83%) in this study. Ajayi et al. (2004) reported AOT as the second most common (19.6%) OT in Nigerian children and adolescents while Adebayo et al. (2002) in another Nigerian study reported the AOT as the third most common OT.

Odontogenic Fibroma (OF)

The WHO describes the OF as a rare benign neoplasm of odontogenic ectomesenchymal origin (Kramer et al., 1992; Philipsen et al., 2005). POF represents the soft tissue counterpart of central odontogenic fibroma (Buchner et al., 2006). In the current study OF and POF accounted for 0.26% and 4.85% of all OTs respectively. In one of very few studies on POF, Ramachandra et al. (2014) reported a relative frequency of 2.63% in India. OFs are extremely rare neoplasms with the reported prevalence ranging from 0.5% to 9.89% (Olgac et al., 2006; Alsheddi et al., 2015).

Odontomas (ODTs)

ODTs accounted for 3.58% of all OTs in this study, which is comparable to the findings of Kebede et al. (2017) who reported a relative frequency of 3.7% in Ethiopia. These results are consistent with those of other studies (Santos et al., 2001; Fernandes et al; 2005; Saghravanian et al., 2010; Nalabolu et al., 2016). In contrast, Mamabolo et al. (2011) reported a prevalence rate of 8.6%. In Nigeria, the reported prevalence of ODTs ranges between 2.2% and 8% (Adebayo et al., 2002; Adebayo et al., 2005) whereas in China, the range is between 4.7% and 6.11% (Jing et al., 2007; Luo and Li, 2009). Latin American studies demonstrated that ODTs are the most common OTs in Brazil (22.1%) and Mexico (30.8%) (Avelar et al., 2008; Gaitan Cepeda et al., 2010). These discrepancies in the prevalence of ODTs in different countries may be underestimated due to the unique clinical features of this tumour (Jing et al., 2007).

The low prevalence of other benign OTs such as OF and CB (one case each) was insignificant and no meaningful conclusions could be drawn. Collectively the tumours

comprised 0.52% of all OTs. Similar results were observed in previous research. (Varkhede et al., 2011).

Malignant OTs

Although less than 100 cases of malignant OTs have been reported internationally, the highest frequency of malignant OTs were observed in Africa and China (Ladeinde 2005; Jing et al., 2007; Luo and Li, 2009; Lawal et al., 2013). Malignant OTs accounted for 1.8% of all OTs in this study. This result matches those of other studies, in Brazil (0.6%), Chile (0.6%) and the USA (0.4%) (Ochsenius et al., 2002; Fernandes et al; 2005; Buchner et al., 2006). Similarly Mamabolo et al. (2011) reported four cases of AMCA in patients who were in the first two decades of life in a rural South African population sample. Lawal et al. (2013) reported a relative frequency of 1.1%, 2.6% and 0.4% in AMCA, PISCC, and AMFS respectively. The rarity, complexity and subsequent inadequate knowledge of the clinicopathogical features of malignant OTs as well as changes in their classification complicates reporting on their prevalence.

4.3 The second objective for this study was to classify OTs seen at Wits Oral Health Centre from 2004 to 2013 in alignment with the 2017 WHO classification of OTs and compare our findings with those reported in literature.

The classification of OTs is based on benign or malignant behaviour. The Benign OTs are grouped OTs with odontogenic epithelium, OTs with odontogenic epithelium and odontogenic ectomesenchyme, and OTs with odontogenic ectomesenchyme (Jordan and Speight, 2009). In this study, 385 OTs were benign and only 7 were malignant tumours. OTs with odontogenic epithelium were the most common (71.95%) benign OTs. Of the epithelial odontogenic tumours AMB was the most common (92.42%) OT followed by AOT (7.58%). Lawal et al. (2013) reported OTs with odontogenic ectomesenchyme as the most common OTs comprising 73.3% of all OTs seen in Nigeria.

Similar findings were reported by Osterne et al. (2011). However, Da Silva et al. (2016) reported 72.3% of OTs to be of odontogenic epithelium as the most common OT. The frequent tumour within the same group was KCOT (34.6%) followed by AMB (32.9%) and ODTs (11.4%) (Da Silva et al., 2016). OTs were the second most common and accounted for 24.42%. This study included the COF as per the 2017 WHO classification. COF (46.8%) was the most common OT followed by OM (30.85%) and POF (20.21%). This is comparable to the findings of Lawal et al. (2013). However, Lawal et al. (2013) reported Fibromyxoma (FM), which comprised 14.7% of all OTs and 88.6% ectomesenchymal OTs. In Brazil, 14.59% ectomesenchymal OTs were the third most common OT (Osterne et al, 2011).

In Brazil, OTs with odontogenic epithelium and odontogenic ectomesenchyme accounted for 35.8% of all OTs and in this group of OTs, complex ODT (17.5%) was the most frequent OT, followed by compound ODT (14.2%) and CCOT (3.8%) (Servato et al., 2013). However, in this study the mixed group of tumours (with odontogenic epithelium and odontogenic ectomesenchyme) contributed 3.64%, towards all OTs and was the least common group of all the benign OTs. Complex ODT (84.71%) was the commonest OT followed by one case of each of the following: The compound ODT (7.14%) and AMBFO (7.14%). Our findings are comparable to those of Lawal et al. (2013) where group 3 lesions (the mixed group) at 6% of cases were the third commonest group of lesions in their study series, although AMBF (4.1%) was the commonest lesion in this group (Lawal et al., 2013).

The classification of Benign OTs is quite user friendly when reporting on the prevalence of benign OTs. However, previous research reports were inconsistent with the application of the 1992 and 2005 WHO classification of OTs. Other studies reported on the prevalence of different benign OT groups of all OTs (benign combined with malignant) whereas in other study series the prevalence of various benign OT groups is reported within the benign OTs only. The variation in the prevalence of OTs may be due the modifications in the WHO classification of OTs.

Malignant OTs

The WHO (2005) classification of OTs, malignant OTs were divided into odontogenic carcinomas and odontogenic sarcomas (Barnes et al., 2005). In the 2017 WHO odontogenic carcinosarcomas were added. The malignant OTs are extremely rare and represented 1.3 –5.2% of the tumours (Daley and Wysocki, 1994; Mosqueda-Taylor et al., 1997; Osterne et al., 2011). In the current study, malignant OTs contributed 1.77% of all OTs. There were four AMCAs and one case of CCOC, SOC, and AMBFS.

In Sri Lanka three cases of AMCA, three cases of odontogenic carcinoma arising from pre-existing cysts and one case of metastasising AMB were reported (Siriwardena et al., 2012). Servato et al. (2013) reported three AMCAs, one PISCC and one CCOC in Brazil. Dhanuthai (2004) reported two OMs and one AMBFS and eleven malignant AMB. However, Kebede et al. (2017) reports 26 cases of PISCC over eight years period in Ethiopia, making it 19.6% of overall OTs. Racial disparities and differences in genetic makeup might be the attributes towards discrepancy in the prevalence of Malignant OTs.

4.4 The third objective was to determine the clinicopathological features of all OTs seen at the Department of Oral Pathology, Wits Oral Health Centre from 2004 to 2013.

Age

In the present study, only one case (OM) was recorded in the first decade of life and these results are comparable to the findings of studies conducted in India (Varkhede et al 2011; Nalabolu et al., 2016). For OTs reviewed retrospectively the age of the corresponding patients at diagnosis ranged from 1 year to 82 years and the incidence of OTs peaked in the second and third decades of life. These results are consistent with those of previous studies from Pakistan and Saudi Arabia (Naz et al., 2014; Asheddi et al., 2015). The mean age recorded in this study was 30.88 years; these observations

are similar to those of studies in other countries (Olgac et al., 2006; Osterne et al., 2011; Nalabou et al., 2016).

Gender

In this study, the OTs were predominantly in females (52%). Similar findings were reported from India (Varkhede et al., 2011). However, these findings are inconsistent with those reported from Pakistan (Naz et al., 2014), India (Kabede et al., 2017) Nigeria (Lawal et al., 2013; Ladeinde, 2005) and Brazil (Avelar et al., 2008; Santos 2001) where cases of OTs were seen more frequently in males than in females. Variation observed in the prevalence of OTs in the two genders may partially be attributed to mismatched efforts in seeking medical assistance between female and male patients. Females tend to consult earlier than males who tend to present late when the disease has progressed further.

Mandible vs Maxilla

Most OTs occur in the mandible, most often in the posterior molar-area whilst a few have a strong predilection for the maxillary anterior sites. In this study, most of the OTs were found to be involving the mandible (80.61%), especially the posterior sites. These observations were similar to many other published research reports (Lu et al., 1998; Olgac et al., 2006; Siriwardena et al., 2012; Nalabou et al., 2016).

Ameloblastoma

In the current study, AMB was the most common OT (65.30%). The distribution of OTs tends to vary with age, gender and site of occurrences. In India, 67.32% of AMB occurred in patients who were in their third and fourth decades of life (Vrakhede et al., 2011; Deepthi et al., 2016). However, in the current study most of AMBs occurred in the third and second decades of life. This is comparable with the findings in a study conducted in Saudi Arabia (Alsheddi et al., 2015). The majority of AMB in the current study were seen most commonly in male patients with a male to female ratio of 1:0.8.

This is consistent with reports from Nigeria (Ajayi et al., 2004; Ladeinde et al., 2005; Lawal et al., 2013) and Ethiopia (Kebede et al., 2017). However, AMBs have been reported to show female predominance in a number of studies (Jing et al., 2007; Ramachandra et al., 2014). In this study, the most common site of involvement for AMB was the posterior mandible. Similar findings have been reported in Nigeria (Ajayi et al., 2004; Ladeinde et al., 2005; Lawal et al., 2013) and India (Deepthi et al., 2016).

Cemento-Ossifying Fibroma (COF)

The COF is a benign fibro-osseous maxillary tumour in the fibro-osseous group of lesions, which includes fibrous dysplasia and cemento-osseous dysplasia (Liu et al., 2010). The WHO (2017) classification of OTs has incorporated COF in tooth bearing areas of the jaws into the ectomesenchymal group of OTs (El-Naggar et al., 2017). In this study, COF is the second (11.22%) most common OT. The peak incidence (12) of COF was the second decade of life. The posterior mandible was the most common site of involvement. The COF is most commonly seen in the third and fourth decades of life and is more frequent in females than in males (4:1). The most common location for COF is the mandible, with 70-90% of all cases presenting in that jaw (Sanchis et al., 2004; Liu et al., 2010), in this study, the COF showed a female predilection with a male to female ratio of 1: 2.1. Most knowledge on COF has been acquired through case reports or small cases series; the body of knowledge available in the literature on COF in association with OTs extremely limited.

Odontogenic Myxoma (OM)

Sirram and Shetty, (2008) reported OM as the third (6.0%) most common OT in India. Similarly OM was the third common OT (7.40%) in this study. The peak incidence of OM was recorded in the third decade of life; the anterior mandible was the dominant anatomical location. Osterne et al. (2011) reported OM as common in female patients between the age of 1 and 33 years with a mean age of 17.1 years; the authors reported a maxilla to mandible ratio of 1.0: 1.4, which is comparable to current results. In contrast

to the findings in this study, Kebede et al (2017) reported OM a male predilection with a male to female ratio of 1:0.4. Lawal et al. (2013) reported no obvious site or gender predilection for OM.

Adenomatoid Odontogenic Tumour (AOT)

The AOT represents 3% to 7% of all OTs and more than 750 cases have been reported in the literature (Neville and Bouquot, 2016). The AOT accounts for 5.36% of all the OTs in this study. Similarly in India, the AOT accounted for 5.5% and 5.83% in two separate studies (Varkhede et al., 2011; Nalabolu et al., 2016). The AOT is commonly seen in younger patients with two-thirds of cases diagnosed in patients in the second decade of life (Neville et al., 2016). Olgac et al. (2006) in Istanbul observed a trend of AOT in young individuals below the age of twenty years. However, Alsheedi et al. (2015) reported AOT to be common in patients who were within their third decade of life. AOT (7) (5.83%) was common in female patients who were in their second decade of life and the common affected site was the anterior part of the maxilla (6) (Varkhede et al., 2011).

In this study, the AOT was more common in males. Arotiba et al. (1997) and Jing et al. (2007) reported a female predominance in Nigeria and China respectively. In India, equal distribution of AOT among males and females has been reported (Ramachandra et al., 2014). The most common site of involvement was the anterior maxilla. In India, the mandible was the most commonly involved jaw (Ramachandra et al., 2014). Jing et al. (2007) reported equal jaw distribution. The AOTs generally do not exceed 3cm in greatest diameter, therefore most are asymptomatic and discovered incidentally (Neville et al., 2016).

Peripheral Odontogenic Fibroma (POF)

Several study series (Lawal et al., 2013; Gaitan Cepeda et al., 2010; Saghravanian et al., 2010) have reported on the prevalence of OF, however POF was not specifically reported on. POF accounted for 4.85% of all OTs in this study, a finding similar to that reported by Ramachandra et al. (2014). The peak incidence was in the fourth decade of life. POF showed a female predilection with a male to female ratio of 1:2.5 and most commonly involved the posterior mandible with a maxilla to mandible ratio of 1:1.7. Ramachandra et al. (2014) reported two cases of POF in two male patients which presented in the posterior mandible. The available literature on POF is limited to allow meaningful comparison.

Odontoma (ODTs)

ODTs, thought to be hamartomatous in nature (Reichart and Philipsen, 2004) they accounted for 3.58% of all OTs in this study, lower than the result reported in Nigeria (8%) (Adebayo et al., 2002). Similar to the findings of a Brazilian study, the ODTs were more common in females (Santo et al., 2001). In contrast, two studies, one in Indian (Ramachandra et al., 2014) and another in Nigeria (Adebayo et al., 2005) reported a male predilection.

However, Varkhede et al., (2011) reported equal gender distribution of ODTs. In this study, ODTs were common in the posterior mandible unlike the findings in Indian studies (Varkhede et al., 2011; Ramachandra et al., 2014; Nalabolu et al., 2016) which reported the maxillary anterior region as the most common site. Due to the asymptomatic nature of ODTs, these neoplasms are diagnosed incidentally in the routine radiographs. This factor may have contributed to the low prevalence of ODTs in this study. Other contributing factors include geographic variation, genetic and environmental influences (Sirram and Shetty, 2008).

There was one case each for CB and OF. Deepthi et al. (2016) reported four cases of CB, with a peak incidence in the second decade and mostly presented in the mandible. Lack of these tumours in the epidemiological data makes it impossible for one to draw comparison. In addition confirms the rarity of these tumours.

Malignant OTs

In the current study, malignant OTs accounted 1.8% of all OTs with four cases of AMCA contributing 1.02% and one case for CCOC, SOC and AMFS each contributing 0.26% respectively. Taghavi et al. (2013) reported seven cases of AMCA in Iran, the tumours were more common in males than females with a mean age of 40.2 years and AMCA was more common in the maxilla than the mandible. In the current study AMCAs were common in the fourth decade of life, show equal distribution across both genders. Three of four cases presented in the posterior mandible and one case in the maxilla.
. A South African study of OTs in a paediatric population reported four cases of AMCA within the first two decades of life, three in males and one in a female. Of the four cases, three presented in the mandible (Mamabolo et al., 2011). The scarcity of reports on CCOC, SOC and AMFS makes a comparative analysis impossible.

4.5 LIMITATIONS OF THE STUDY

This being a cross-sectional study, the results cannot be generalised to the entire population of South Africa (SA). Only one study was conducted in SA (Mamabolo et al., 2011), hence local literature available for comparison of findings is minimal. A few of the patient reports had missing or inadequate data from the retrieved archives. The researcher did not include race and geographic locations as part of the socio demographic variables because the data was not available in the vast majority of patient records

4.6 CONCLUSIONS

The study showed 392 cases of OTs out of 13665 total numbers of oral lesions between 2004 -2013. In this study 385 OTs were benign and only seven were malignant tumours. Benign OTs with odontogenic epithelium contributed 71.95%, OTs with odontogenic ectomesenchyme accounted for 24.42% and the mixed group (odontogenic epithelium with odontogenic ectomesenchyme,) contributed 3.64%, towards all benign OTs. The present study has reported on the prevalence of various OTs with AMB (65.30%) as the most predominant OT followed by COF (11.22%) and OM (7.40%). OTs are not

commonly seen at the Wits Oral Health Centre. Most OTs occurred in the second (23.21%) and third (31.12%) decades of life. OTs showed a slight female predilection with a male to female ratio of 1: 1.1. The posterior mandible was the most commonly involved site with a five-fold increase in mandibular involvement. This finding is largely consistent with slight variation with those of studies conducted in Asia and Africa. The observed variation is largely attributed to the 2017 WHO reclassification of OTs.

4.7 RECOMMENDATIONS

Oral Health Care Practitioners should be upskilled and the importance of good medical record keeping should be emphasised. Comprehensive patient histories should be documented in patient medical records to facilitate retrieval of information for research purposes. A user-friendly software system is recommended to keep patient records electronically to avoid loss of patient information due to missing or misplaced files. In the future, multicentre studies incorporating external factors such as socioeconomic status, that may be contributory to the variance in OTs relative frequencies are recommended, to allow extrapolation of the information to the South African population and to enable improved comparisons with other international series.

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6. ANNEXURES

6.1 Annexure A (Data sheet)

Case number	Age	Gender (Male or Female)	Maxilla(anterior, premolar or Molar)	Mandible(anterior, premolar, Molar, angle or ramus)	Other(specify)	Diagnosis

6.2 Annexure B: Letter to request permission to the head of the Department of Oral Pathology, Wits School of Oral Health Sciences, University of Witwatersrand

University of Witwatersrand
Department of Oral Pathology
7 York Road
Parktown
0028
29 May 2015

Dr SP Ngwenya
The Head of Department of Oral Pathology
Wits School of Oral Health Sciences
University of Witwatersrand, Johannesburg
Dear Dr SP Ngwenya

RE: PERMISSION REQUEST TO CONDUCT A RESEARCH STUDY

I am a Masters student in Dental Sciences at the University of Witwatersrand, and I like to request your permission to conduct research in the Department of Oral Pathology, Wits School of Oral Health Sciences. The proposed title of my study is: Odontogenic Tumours: A 10 year retrospective study in a South African teaching hospital. The aim of the study is to determine the relative frequency of odontogenic tumours diagnosed in the Department of Oral Pathology from 2004 to 2014 Wits School of Oral Health sciences.
Should you require any clarification regarding the aforementioned, you can kindly contact me on: Tel/Cell: 011 717/0824079192 E-mail: mpatikana.galane@wits.ac.za.
I would be grateful if my request will be accepted.

Thanking you in advance.

Yours Sincerely

Dr ML Galane

6.3 Annexure C: Letter to request permission to the Head/CEO of Wits School of Oral Health Sciences and Wits Oral Health Centre

University of Witwatersrand
Department of Oral Pathology
7 York Road
Parktown
0028
29 May 2015

Prof P Hlongwa
The director / the Head of Wits School of Oral Health Sciences
University of Witwatersrand
Dear Professor P Hlongwa

RE: PERMISSION REQUEST TO CONDUCT A RESEARCH STUDY

I am currently studying towards my Master degree in Dental Science at the University of Witwatersrand, Johannesburg. I hereby request permission to conduct study in the department of Oral pathology, Wits School of Oral Health Sciences in partial fulfilment towards the MScDent degree.
The proposed title of my study is: Odontogenic Tumours: A 10 year retrospective study in a South African teaching hospital. The aim of the study is to determine the relative frequency of odontogenic tumours diagnosed in the Department of Oral Pathology from 2004 to 2014 Wits School of Oral Health sciences.

This study will be conducted under the supervision of Dr SP Ngwenya, the Head of the Department of Oral Pathology, Wits School of Oral Health sciences. Should you require any clarification regarding the aforementioned, you can kindly contact me on: Tel/Cell: 011 717 2139/0824079192 E-mail: mpatikana.galane@wits.ac.za.

I would be grateful if my request will be accepted. Thank you for assistance.

Yours Sincerely

Dr ML Galane

6.4 Annexure D: Permission letter from the Head/CEO of Wits School of Oral Health Sciences and Wits Oral Health Centre

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

WITS Oral Health Centre
Private Bag X15, BRAAMFONTEIN, 2017
Enquiries: Ms ME Huygen
Tel: 011 717 2130
Fax: 086 765 4436
e-mail: Liza.Huygen@wits.ac.za

September 8, 2015

Dr ML Galane
School of Oral Health Sciences
University of the Witwatersrand
Johannesburg

Regarding: "Odontogenic Tumours: A 10 year retrospective study in a South African teaching hospital."

Reference: HREC/SEP2015/03

It is my pleasure to grant final approval access Wits Oral Health Centre Patient records in order to conduct your research with the above title. The Hospital Research and Ethics Committee allocated a unique reference number to this application - Kindly quote this reference number in all future correspondence regarding this research topic.

Please note that the Hospital Research and Ethics Committee should be informed of the estimated date the research will commence, as well as regular status reports until the research have been concluded. Within a month after conclusion of the research project, a written report must be submitted to the Head of School / CEO, summarizing the final results / outcome as well as recommendations made based on the research conducted.

Regards,

Prof P Hlongwa
CEO / Head of School

6.5 Annexure E: Human Research Ethics Committee (Medical) Clearance Certificate

R14/49 Dr Galane Mpatikana Leslie

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150828

NAME: (Principal Investigator)	Dr Galane Mpatikana Leslie
DEPARTMENT:	Oral Pathology School of Oral Health Science
PROJECT TITLE:	Odontogenic Tumours: A 10 Year Retrospective Study in a South African Teaching Hospital
DATE CONSIDERED:	28/08/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Sizakele Ngwenya

APPROVED BY: Professor P Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 02/09/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date 02/09/2015

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

6.6 Annexure F: Turnitin Report

Dr

ORIGINALITY REPORT

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SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

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