CLINICO-PATHOLOGICAL PATTERN OF ODONTOGENIC NEOPLASMS AT TWO NATIONAL REFERRAL CENTRES IN NAIROBI, KENYA

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SUPERVISOR'S APPROVAL

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DEDICATION

This is for the glory of God. To my late father, Mark Kevogo Kezegule, whose guidance, support and encouragement made me believe in staying strong up to the finish line. Thank you, baba, for being my greatest cheerleader. And to my wife Doris who has been a pillar of strength throughout my journey in postgraduate studies.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

AC	Ameloblastic carcinoma
AF	Ameloblastic fibroma
AOT	Adenomatoid odontogenic tumour
CCOC	Clear cell odontogenic carcinoma
CT scan	Computed tomographic scan
DCE-MRI scan	Dynamic contrast enhanced-magnetic resonance imaging scan
KCOT	Keratocystic odontogenic tumour
KNH	Kenyatta National Hospital
MRI	Magnetic resonance imaging
OF	Odontogenic fibroma
OM	Odontogenic myxoma
ON/ONs	Odontogenic neoplasm(s)
OPG	Orthopantomogram
SPSS	Statistical Package for the Social Sciences
UNDH	University of Nairobi Dental Hospital
WHO	World Health Organisation

OPERATIONAL DEFINITIONS

Hamartoma - is a benign (non-cancerous) tumour-like malformation made up of an abnormal mixture of cells and tissues found in areas of the body where growth occurs. It is considered a developmental disorder.

Aetiology - refers to cause

De novo - from the beginning (anew)

ABSTRACT

Background:

Odontogenic neoplasms (ONs) are lesions with insidious progress but tend to cause disfigurement and high surgical morbidity. The prevalence in Africa is about 9-69%. Knowledge of their trend and pattern of presentation both clinically and pathologically is of utmost importance. The paucity of data in Kenya necessitated the present study which entailed an audit of patients' records over a period of 7 years extending from January 2012 to December 2018. It evaluated the clinical and pathological pattern of presentation of odontogenic neoplasms at the Kenyatta National Hospital (KNH) and the University of Nairobi Dental Hospital (UNDH) to demonstrate the current trends in the pattern of their presentation.

Objective:

The main objective was to retrospectively describe the clinical and pathological pattern of odontogenic neoplasms seen at the KNH and the UNDH between January 2012 and December 2018.

Materials and methods:

This was a descriptive retrospective research design. The study sample comprised of records of patients who presented and were diagnosed with jaw neoplasms at the KNH and the UNDH from 1st January 2012 to 31st December 2018.

A specially designed data collection form was used to record relevant information to the study including age, gender, nationality, race, primary or recurrent neoplasm anatomical site, duration, symptoms and histological diagnosis. The data collected were analysed using statistical package for the social sciences (SPSS). Both descriptive and inferential statistics were used to interprete the data. Frequencies, percentages, means and standard deviations were used to describe the patterns of the investigated study variables.

Inferential statistics included Chi-square and independent t-test. Chi-square was used to determine relationships between the participants' demographic characteristics (age, gender, nationality, race, and home area) and primary neoplasm, recurrent neoplasm, anatomical site of the disease and duration of neoplasms. On the other hand, the independent t-test was used to determine whether there was a statistically significant

difference between the gender and ages of patients with ONs during the study period.

Results

There were 372 cases of ONs that were diagnosed at the KNH and the UNDH. These comprised 47.6% of all jaw lesions at the two centres. The age range of the cases was 5.5-77 years with a mean of 30.165(SD±15.15.77). The peak age of occurrence of ONs was the 3rd decade of life. The male to female ratio was 1:1.1. Most of the cases (220, 60.8%) originated from rural areas. ONs were predominantly benign (369 cases, 99.2%), while the malignant ones were rare (3 cases, 0.8%). Primary ONs were 351 cases (94.4%) while recurrent ONs were 21 cases (5.6%). The mandible was the predominantly involved site (295 cases, 79.3%), with mandible to maxilla ratio having been 4:1. ONs in the maxilla commonly occurred in the anterior region. Swelling was the commonly reported symptoms in 360 cases. Other symptoms included tooth mobility, mal-aligned/displaced teeth, pain, secondary infection, unerupted teeth and rarely ulceration. Most cases presented between 1 to 5 years following the onset of symptoms. Ameloblastoma was the most common ON (242 cases, 65.1%). Other ONs seen in this study included cemento-ossifying fibroma (40 cases), odontogenic myxoma (35 cases), odontoma (27 cases), adenomatoid odontogenic tumour (17 cases), ameloblastic fibroma (4 cases), odontogenic fibroma (4 cases), clear cell odontogenic carcinoma (2 cases) and ameloblastic carcinoma (1 case). Ameloblastoma had the follicular type (51 cases) as the commonest histologic subtype. Other subtypes were the plexiform (44 cases), cystic (42 cases), granular (1 case) and mixed (35 cases). The odontoma had the complex subtype reported in only two cases.

Conclusion

ONs are common jaw lesions in patients aged below 40 years who presented at the KNH and the UNDH. The posterior mandible was the most involved site. In the maxilla, the anterior region was commonly involved. Ameloblastoma was the most common ON.

Recommendations

The creation and implementation of policies in the public health system that will impact on the diagnosis and management of ONs by bringing specialized medical services closer to the population such as in the rural areas. In addition, there should be sensitization of the citizenry on the occurrence of ONs, the long-term effect, and the need to seek early treatment (less than 1year since the onset of symptoms).

CHAPTER ONE

1.1 Background Information

A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change [1]. Lesions originating from the odontogenic epithelium and remaining entrapped either in adjacent soft tissues or within the jaws include odontogenic neoplastic lesions and odontogenic cysts [2].

Odontogenic neoplasms (ONs) are a group of heterogeneous lesions that arise from dental/tooth forming tissues that include the epithelium and ectomesenchyme. They usually present with variable clinical behaviour and histopathological types. They comprise a range of hamartomatous to malignant lesions [3]. These neoplasms represent inductive interactions between the odontogenic ectomesenchyme and epithelium, with degenerative changes in the tooth-forming tissues [3, 4]. They may be central/intraosseous (found within the jawbones) or peripheral/extraosseous (found in the mucosal tissue overlying tooth-bearing areas). They are primarily categorized as benign or malignant.

The specific aetiology of these neoplasms is unknown. Benign forms seem to arise *de novo* while malignant forms may arise de novo or from their benign precursors [5]. Growth factors like bone morphogenetic protein and fibroblast growth factor play a major role in organogenesis and specifically in odontogenesis. They are also believed to have a role in oncogenesis [6].

ONs have a varied pattern of growth and invasiveness. Generally, they are slow-growing causing distortion of bone by resorption of the trabeculae of the medullary space and expansion of the cortical bone. Eventually they present as painless swellings or as asymptomatic lesions detected during a routine dental radiographic assessment of the oral cavity. Pain is commonly present in infected neoplasms while paraesthesia of the lips or tongue is uncommon [7].

Large neoplasms may exhibit much more aggressive behaviour that includes extensive destruction of bone and proliferation into the soft tissues. When benign but

aggressive neoplasms like ameloblastoma gain access to the soft tissues they may become impossible to eradicate successfully [7].

Generally, ONs exhibit gradual jaw expansion/extension, altered bone density, bone resorption, root resorption, tooth mobility, disfigurement in the contiguous tissues and paraesthesia. However, the most common clinical symptom of malignant ONs is pain with consequent rapid swelling [2]. The histological appearance of ONs may mirror one of the stages of the tooth formation process. Extracellular substances may calcify due to epithelial-mesenchymal interactions. Thus, may appear radiolucent, radiopaque or mixed radiopacity on radiographs depending on the types of neoplasm and the extent of calcification [8]. The diagnosis of ONs is based on clinical history, examination, radiological imaging and histopathological examination entailing microscopy and immunohistochemistry.

The imaging modes applied to aid in the diagnosis of ONs include plain radiographs such as the orthopantomogram (OPG) and cross-sectional imaging such as the computed tomography (CT) scan and magnetic resonance imaging (MRI). The OPG and CT scan demonstrate the bone well. The diagnostic value of MRI in ONs is of limited other than where soft tissue neoplasms (extraosseous) occur and in distinguishing between ameloblastoma and keratocystic odontogenic tumour (KCOT - cystic with no solid content). Dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI) scan was found to have been useful in the diagnosis of odontogenic fibroma and myxoma in terms of cystic component uniformity [9].

Classification of ONs is essentially based on the interactions between odontogenic ectomesenchyme and epithelium. The WHO classification is widely accepted and applied [10].

During the management of ONs, the goals entail complete eradication of the neoplasm and preservation of normal tissue which should be done to minimize morbidity. In addition, reconstruction should be performed to replace tissue loss, restore form, rehabilitation and restoration of function with long-term follow-up for early detection of recurrence [11].

ONs have a global prevalence of 2.2-69% of all biopsied lesions in oral pathology laboratories. The developed countries seem to have lower prevalences as compared to

developing countries. Although retrospective studies have been conducted in Africa, Asia, Europe and America, unanswered questions still remain about the relative frequency and the incidence of certain ONs [12-21].

The geographical distribution of ONs is variable. Many studies in different parts of the world have shown differences in the relative prevalence of these neoplasms. However, there is a lack of a comprehensive database for ONs in Kenya. In addition, proper allocation of public health care resources for awareness programs, intervention, rehabilitation after surgery and research requires quantification of both disease current burden and the trend in its impact.

The aim of this study was to describe the current trends of ONs in terms of socio-demographic distribution, clinical presentation (signs and symptoms, and anatomical distribution) and the histological diagnosis variations.

1.2 Literature review

ONs show a higher incidence in the African population in the sub-Saharan region. Multiple studies conducted in this region have alluded to this occurrence [12-17]. However, there is a paucity of information on patterns of occurrence in Kenya.

A systematic review conducted in 2017 of data from 14 sub-Saharan Africa countries looked at 4,384 cases of ONs. These included 2186 African cases presented at the International Association of Oral and Maxillofacial Pathologists (IAOP) Congress in Cape Town, South Africa in 1998 and 2198 cases reported in the published scientific literature from 1998 to 2016. The commonest ON was ameloblastoma (86.9%) followed by keratocystic odontogenic tumour (KCOT, 6.9%) and odontogenic myxoma (4.9%). Malignant ONs formed 1.4%. Nigeria contributed 38.7% of the cases in the ONs series [12].

A 2012 Kenyan study carried out at the University of Nairobi division of Oral Pathology/Oral Medicine looked at 4257 biopsies from a period of 19 years (1992-2011). Of these, 597 (14.02%) were jaw bone neoplasms. Out of this number, 417 (69.85%) were ONs while 180 (30.15%) were other bone-related neoplasms. No gender predilection was demonstrated. The age range of the cases with ONs was between 5-85yrs with a peak at 11-50yrs [13]. The ONs were categorized as of epithelial origin (346 cases, 83%), and mesodermal origin (36 cases, 8.6%) and mixed origin (34 cases, 8.2%). ONs of epithelial origin were ameloblastoma (274 cases, 65.7%), KCOT (67 cases, 16.1%), calcifying epithelial odontogenic tumour (5 cases, 1.2%) and adenomatoid odontogenic tumour (1 case, 0.2%) [13]. ONs of mesodermal origin included odontogenic myxoma (29 cases, 7%) and cementoma (7 cases, 1.8%). ONs of mixed origin included odontoma (16 cases, 3.8%), ameloblastic fibroma (7 cases, 1.8%), myxofibroma (6 cases, 1.4%), calcifying cystic odontogenic tumour (4 cases, 1%) and amelofibro-odontoma (1 case, 0.2%) [13].

A study conducted in Ethiopia (2017) at the dental and maxillofacial department of St. Paul's referral hospital in Addis Ababa demonstrated a male predilection of 54% (88 males) as compared to the female of 46% (75 males). The mean age of ONs occurrence was 34yrs with an age range of 8-80yrs. This study showed that the benign types were more frequent (132 cases, 81%) as compared to the malignant types (31 cases, 19%). The mandible was the commonest site of occurrence at 77.3% (126

cases) as compared to the maxilla at 22.7% (37 cases) [14]. Ameloblastoma (75 cases, 46%) was the most common benign neoplasm. Others in descending order included odontogenic myxoma (14%), KCOT (10%), odontogenic fibroma (10%), ameloblastic fibroma (9%), odontoma (6%) and others not specified (9%) [14].

In the Oral Pathology Department of the University College of Ibadan, records of 21yrs (1990-2011) were reviewed (2013). Of the 638 jaw lesions diagnosed, 266 (41.7%) were ONs. Benign forms were 255 cases (95.9%) while malignant forms were 11 cases (4.1%). The age range of occurrence was 3-82yrs with a peak in the 3rd decade of life. They occurred more in the mandible than in the maxilla with a ratio of 5:1. Gender analysis showed male preponderance with a male to female ratio of 1.2:1 [15]. A complementary study in children and adolescents (2013) was done. There were 147 cases of jaw swellings that were seen in those aged 19 years or less during the study period, out of which 48 (32.7%) were ONs. Males were more affected with a male: female ratio of 7:5. The mandible (108 cases) was the commonest site of occurrence with a mandible: maxilla ratio of 11:4. Ameloblastoma was the most common with 14 cases (29.1%) solid ameloblastoma and 9 (18.8%) cystic ameloblastoma cases. This was followed by odontogenic fibromyxoma with 8 (16.7%) cases. Calcifying epithelial odontogenic tumour, calcifying cystic odontogenic tumour, and odontogenic fibroma were also seen [16].

A review study in 2011 on ONs was conducted at the University of Limpopo in South Africa over a period of 26 years in patients within the 1st and 2nd decades of life. This showed that 254 of the 743 cases (33%) of ONs occurred in this age-group. Of these, 250 cases (98.4%) were benign while 4 cases (1.6%) were malignant. The mandible was the most common site (164 cases, 65%) while the maxilla had 90 cases (35%). There was a male predilection with a male (126 cases) to female (118 cases) ratio of 1:1.1. The most common ON in the first two decades of life was ameloblastoma (43%) [17].

In Southern India, the incidence of ONs was found to have been 2.17% (161 of 7400 oral biopsies) in a 2017 study. The cases occurred in the age range of 1-70 years with the 3rd and 4th decades of life being of peak incidence. There was a male to female ratio of 1.43:1 (95 males - 69% to 66 females - 41%). The mandible (116 cases, 72%) was more involved than the maxilla (45 cases, 28%). The ratio of involvement for the

posterior to anterior regions for the mandible and the maxilla was 2.8:1 and 1:1.3 respectively. The commonest ONs included ameloblastoma (79 cases, 49%), KCOT (53 cases, 32.09%), odontomas (10 cases, 6.2%) and AOT (9 cases, 5.5%). Others ONs recorded in the study included odontogenic myxoma (4 cases, 2.4%), calcifying epithelial odontogenic tumour (3 cases, 1.8%), squamous odontogenic tumour (2 cases, 1.2%)], ameloblastic fibroma (1 case, 0.6%) [18].

Studies among the Chinese found 1309 cases of ONs recorded over a period of 21years (1985-2006) at the Peking University of Stomatology and analysed in 2009. These neoplasms formed 3.92% of all pathologic specimens in the oral pathology laboratory. The benign ONs comprised 94.4% while the malignant ones were 5.6%. The common benign neoplasms included KCOT (38.73%), ameloblastoma (36.52%) and odontomas (6.11%) [19].

In South America, a study was carried out in North-eastern Brazil in 2018 at the Federal University of Rio Grande do Norte oral pathology laboratory. They looked at 10,970 oral and maxillofacial lesions. These were records of cases over a 22-year period from 1996 to 2017. There were 247 cases (2.3%) of ONs of which 245 cases (99.2%) were benign and 2 cases (0.8%) were malignant. There was a female predilection (136 cases, 55%) with a male to female ratio of 1:1.2. The age range of occurrence was 5-81 years with a peak in the 2nd and 3rd decades of life. The malignant types occurred in the 5th and 6th decades of life. The mandible (162 cases, 66%) was the commonest site of ONs, with the posterior region having been more affected (98 cases, 60.5%) [20]. The maxilla had 79 cases (32%) while the anatomical site of 6 cases was not indicated. It was noted that the odontomas and the adenomatoid odontogenic tumours occurred more commonly in the anterior maxillary region. Among the benign types, epithelial neoplasms were 127 cases (51.4%), mixed neoplasms were 94 cases (38.1%) and the mesenchymal neoplasms were 24 cases (9.7%) [20].

An Italian study in 2017 at two university hospitals looked at 344 surgical specimens that included 277 cases of primary neoplasms and 67 cases of recurrences. In the primary neoplasms, there were 185 odontogenic keratocysts (66.8%), 49 ameloblastomas (17.7%), and 40 other benign ONs (14.4%). Ameloblastic carcinomas made up 1.1% (3 cases). The mean age was 46.7 years. The male to

female ratio was 1.8:1. The mandible was the most common site of localization, with 211 cases (76.2%). There were 21 cases of peripheral ONs with ameloblastomas having been the most common (8 cases, 38.1%) [21].

An Egyptian study in 2019 examined records of 215 neoplasms in the department of oral and maxillofacial surgery of the faculty of dentistry in Alexandria University. There were 26 cases (12.06%) of ONs reported among these neoplasms. The females 15 (57.69%) while the males were 11 (42.31%). The age range was 7-73 years with a mean of 34 years. Benign neoplasms were 88.46% (23 cases) while 11.54% (3 cases) were malignant. The mandible to maxilla ratio was 1.2:1. The odontoma was the most common ON followed by ameloblastoma (4, 15.38%), cemento-ossifying fibroma (3 cases), odontogenic myxoma (2 cases), odontogenic fibroma (2 cases) and ameloblastic fibroma (2 cases). Ameloblastic carcinoma was the only malignant ON with 3 cases reported [22].

A 2013 Iranian study showed 188 cases of ONs being 26.1% of all oral and maxillofacial lesions examined. ONs of epithelial origin were 70.6%, while those of mesenchymal and mixed origin were 17.5% and 12.2% respectively. The peak age of ONs was 2nd decade of life. There were 104 male cases while 84 female cases. The male to female ratio of 1.24:1. The mandible was the predominant site with a maxilla to mandible ratio of 1:2.8 [23].

In 2016 a 40-year audit on ameloblastomas was conducted in Iran. This study showed a male predilection. The peak age of these lesions was in the 3rd decade of life. The mandible was the predominant site for the neoplasms. The most common histologic subtypes were the plexiform and follicular patterns [24].

A 2017 epidemiological study of ameloblastomas in south east Asia was conducted by Intapa et al. There was a male to female ratio of 1.4:1. The mean age of patients was 31.3years with a peak in 2nd decade of life. The posterior mandible was the predominant site. Most common histologic subtype was the plexiform type. Others included the follicular and acanthomatous types [25].

1.3 Statement of the problem

ONs are fairly common lesions of the oral and maxillofacial region in Africans as evidenced in the literature from the region. They present a diagnostic challenge due to overlapping clinical and histological features. In sub-Saharan Africa, the late presentation of disease poses a challenge in the management and subsequent outcomes. Moreover, the disfiguring nature of large neoplasms, high cost of reconstructive surgery and risk recurrent disease is a concern to the patient, family, and caregivers. The paucity of data on ONs in our country is evident despite the improved documentation in our national referral centres.

1.4 Justification of the study

There is a need to analyse the clinical and pathologic pattern of ONs and look into their in-depth details so as to have a clear understanding of the epidemiology and the various types of neoplasms that occur in our population.

Emerging trends will guide the shaping of policy in relation to diagnosis and management of ONs. This will lead to the early intervention by the clinicians thus avoid neoplasm presentation in late stages by appropriate management to restore function, aesthetics and eliminate the risk of recurrence.

1.5 Research question

What is the current pattern of ONs as seen in patients presenting for treatment at the KNH and the UNDH?

1.6 Objectives of the study

1.6.1 General Objective

To describe the clinical and pathological patterns of ONs at Kenyatta National Hospital (KNH) and the University of Nairobi Dental Hospital (UNDH).

1.6.2 Specific objectives

1. To describe the proportion of various types ONs in the jaws as seen in KNH and UNDH from January 2012 to December 2018.
2. To describe the clinical presentation, anatomical features and histological variants of ONs.

1.7 Perceived benefits

1. The study will help advance the knowledge on the patterns of occurrence and histopathologic variations of ONs.
2. The study will influence the policy shaping in relation to diagnosis and management of ONs.

CHAPTER TWO

METHODOLOGY

2.1 Study design

This is a retrospective descriptive study.

2.2 Study area

The study was conducted in the histopathology laboratory at the KNH and in the oral pathology laboratory at the UNDH.

KNH is the largest teaching and referral hospital in Kenya. It offers tertiary medical services hence receives referrals from all the major regional and county referral hospitals mainly from the central, eastern, northern, southern and coastal regions of Kenya. Medical equipment and specialist staffing are the highest among public health institutions. The hospital has a dental unit where all patients with dental and maxillofacial conditions are attended to. It registers about 100 new patients every day (5 working days per week). The unit has a department of surgery that is staffed with five consultant oral and maxillofacial surgeons, eight residents (currently), two senior dental officers and a varied number of dental officer interns. There is one oral pathologist working for the hospital. The oral/maxillofacial specimens from the unit and theatre are processed and examined at the general histopathology laboratory; there is no dedicated oral pathology laboratory. The specimens from the unit/theatre are examined microscopically majorly by the oral pathologist but a few are examined by general pathologists.

The UNDH is a teaching hospital. It is purely a dental hospital offering general and specialist dental services. Among its departments are the department of oral and maxillofacial surgery, oral pathology and oral medicine with three thematic units which include include oral and maxillofacial surgery, oral pathology and oral medicine, and oral and maxillofacial radiology. It is staffed with consultant oral and maxillofacial surgeons, eight residents (currently), three oral pathologists and one oral and maxillofacial radiologists. The department offers both out-patient and inpatient consultation/surgical services. It has a dedicated oral pathology laboratory that

handles specimens from within the hospital and also from other hospitals and clinics within the country.

2.3 Study period

The study encompasses the 7-year period running from January 2012 and December 2018.

2.4 Study population

This included the study of records of patients who presented at the KNH and the UNDH with ONs.

2.5 Inclusion criteria

All records of patients with ONs who presented to KNH and the UNDH between January 2012 and December 2018.

2.6 Exclusion criteria

Records of patients seen at the two facilities before January 2012 and after December 2018.

Patients who were seen within the study period but with incomplete medical records.

2.7 Sample size determination

The desired sample size was determined using Fisher's formula [26]:

$$n = \frac{Z^2 pq}{e^2}$$

Where:

n - the desired sample size when the study population is >10,000)

z - the standard normal deviate (set at 1.96 corresponding to a confidence level of 95%)

p - the proportion in the target population to have a specific characteristic (Kenyan study by Butt FMA *et al.*, 2012) - 69.85%

q - 1-p

e - the desired level of precision; set at 0.05 corresponding to a z value of 1.96

Using the formula, the sample size is computed as follows:

$$n = \frac{1.96^2 \; x \; 0.6985 \; x \; (1 - 0.6985)}{0.05^2} = \mathbf{324}$$

A total of **372** records of patients with ONs who presented at KNH and the UNDH between January 2012 and December 2018 were retrieved for the purpose of the study.

2.8 Sampling method

A convenience sampling method was applied in this study.

2.9 Variables

2.9.1 Socio-demographic variables

1. Age
2. Gender
3. Race

2.9.2 Independent variables

1. Anatomical site of neoplasm
2. Duration of neoplasm
3. Primary neoplasm
4. Recurrent neoplasm
5. Symptoms: -
    i. Swelling
    ii. Pain
    iii. Tooth mobility
    iv. Trismus
    v. Paraesthesia
    vi. Secondary infection

2.9.3 Dependent variable

1. Histological diagnosis

2.10 Data collection tools and techniques

The primary researcher was assisted in collecting data by 3 research assistants who were well trained before the commencement of the study. The research assistants comprised of two oral pathology laboratory technologists with postgraduate training and one dental officer intern with an undergraduate degree.

Data were collected with a specially designed data collection sheet, where all the information from patients' records was entered into by a research assistant and the principal investigator.

The recording of individual odontogenic neoplasm was done utilizing the WHO 2017 classification. The socio-demographic and clinical presentation information was obtained from the patients' hospital files.

2.11 Ethical considerations

1. Approval from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC) before the commencement of the study obtained.
2. Permission to access patients' records was granted by the respective managements of KNH and the UNDH.
3. Information derived from the clinical/laboratory records was regarded as confidential and was only used for the purposes of this study.
4. Names of the patients and other personal details were not recorded in the data collection sheet.
5. The findings of this study shall be published and disseminated through journals for the benefit of interested clinicians for the purpose of benefiting the patient(s).

2.12 Data entry, analysis and presentation

Data obtained from patients' hospital records and recorded in the data collection form were entered in the statistical package for the social sciences (SPSS) with WHO disease codes (CD-10 codes) for analysis. Descriptive and inferential statistics were used in the study.

Descriptive statistics included frequencies, percentages, means and standard deviations. Frequencies and percentages were used to analyse the demographic characteristics of the patients with ONs such as age, gender, home area, nationality, and race. Moreover, frequencies and percentages were used to establish the pattern of the primary neoplasm, recurrent neoplasm, symptoms, duration, histological diagnosis, and histological subtype exhibited by patients with odontogenic neoplasms from January 2012 to December 2018 at the two medical centres. Also, the mean and

standard deviations were used to express the average age of patients with odontogenic neoplasms. The standard deviations were used to determine the variations in the mean age of patients.

Inferential statistics included Chi-square and the independent samples t-test. Chi-square was used to test the relationships between the participants' demographic characteristics (age, gender, nationality, race, and home area) and primary neoplasm, recurrent neoplasm, anatomical site of the disease and duration of neoplasms.

The independent samples t-test was used to determine whether there is a statistically significant difference between gender and age of patients with ONs within the retrospective period considered in the study.

The analysed data were presented in the form of tables, pie charts, and graphs.

2.13 Main outcome measures

1. The Socio-demographic pattern of occurrence ONs.
2. Variability of clinical presentation features.
3. Histopathological variants of ONs.

2.14 Study results dissemination

The study findings shall be published in a peer-reviewed journal where clinicians shall be able to access subject to the regulations of the journal.

The findings shall also be submitted to the University of Nairobi repository where access by interested parties is unlimited.

2.15 Difficulties encountered

1. Missing of patients' records
2. Poorly or illegibly recorded data

2.16 Minimizing Error and Biases

1. Pretesting of data collection form was done
2. Utilization of complete patients' records

CHAPTER THREE

RESULTS

3.1 Proportion of odontogenic neoplasms

There were 782 biopsies of jaw lesions that were presented at the KNH and the UNDH over a period of 7 years of which 372 cases were ONs. These cases accounted for 47.6% of all the biopsies. Out of the 372 cases, 369 and 3 were benign and malignant neoplasms respectively (figure 1 and 2).

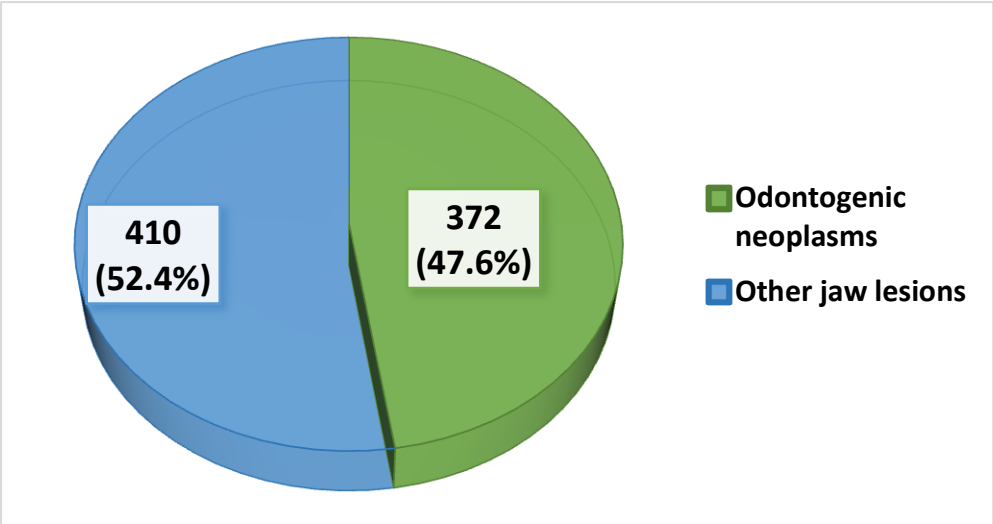

Figure 1: Shows proportion of odontogenic neoplasms in the jaws

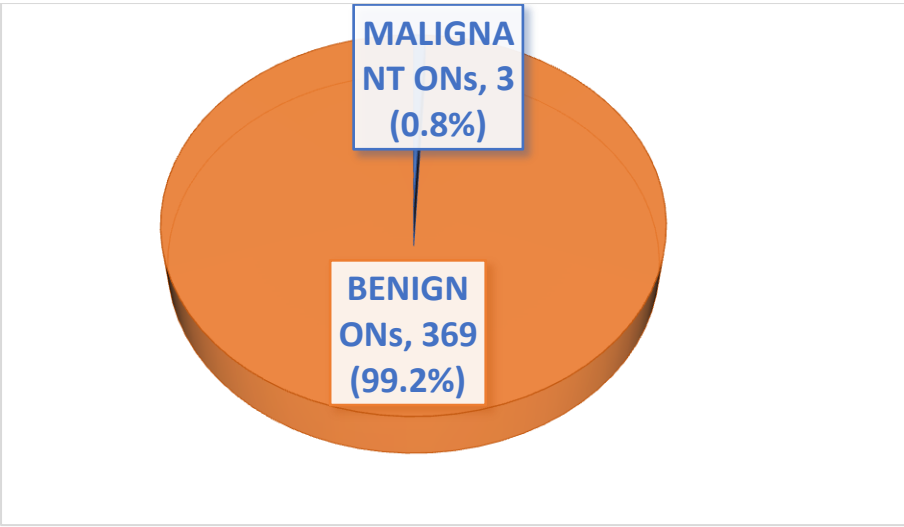

Figure 2: Proportion of odontogenic neoplasms amongst themselves

3.2 Demographic characteristics

3.2.1 Gender and age distribution of patients with odontogenic neoplasms

A total of 372 cases with ONs from January 2012 to December 2018 were included in the present study of whom 170(45.7%) were male and 202(54.3%) were female with an overall age range of 5.5 to 77.0 years. The overall mean age for the patients was 31 years (SD = ±16).

Among the males, the age range was 5.5 to 77.0 years (Mean = 31 years, SD = ±16), while among the females it was 8.0 to 76.0 years (Mean = 31 years, SD = ±15). This was not statistically significant (Levene's Test for Equality of Variances F (356) = 0.641, p-value > 0.05).

The 20 to 29-year-olds were the most affected (28%) followed by the 10 to 19-year-olds (22.6%). Majority of the patients (71.8%) with ONs were below the age of 40 years with those above 70 years having been less affected (1.9%). Fifteen cases were recorded as adults. The frequency of ONs according to age-groups is shown in table 1.

Table 1: Distribution of ONs according to age group

	Frequency	Percent	Cumulative Percent
0 to 9 years	13	3.5	3.5
10 to 19 years	84	22.6	26.1
20 to 29 years	104	28.0	54.1
30 to 39 years	66	17.7	71.8
40 to 49 years	34	9.1	80.9
50 to 59 years	31	8.3	89.2
60 to 69 years	18	4.8	94.0
70 to 79 years	7	1.9	95.9
Specified as adult	15	4.0	100.0
Total	**372**	**100.0**	

3.2.2 Location of residence distribution of patients with odontogenic neoplasms

Regarding the residence distribution of patients with ONs, majority (60.8%) of the cases were from rural areas while those from urban settings accounted for 37.6%. In addition, there were 1.6% of the cases whose residential areas were unspecified as illustrated in Figure 3.

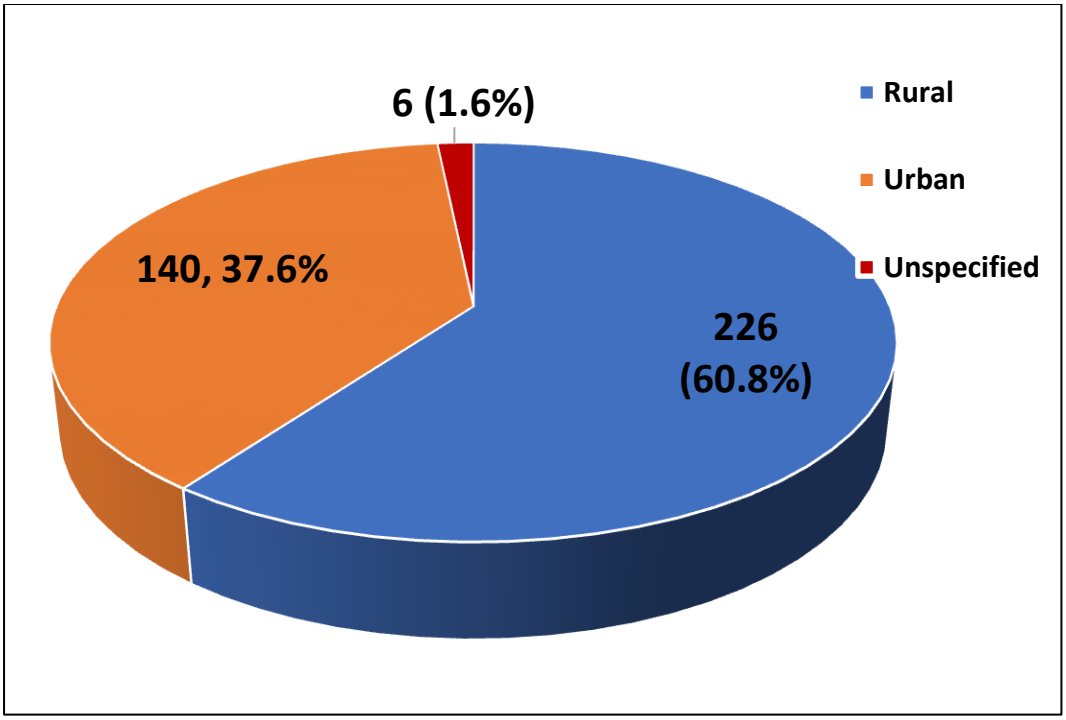

Figure 3: Distribution of ONs according to the case residence

3.3 Pattern of occurrence of ONs

Regarding the occurrence of ONs, 94.4% were primary neoplasms while 5.6% were recurrent neoplasms as illustrated in Figure 4.

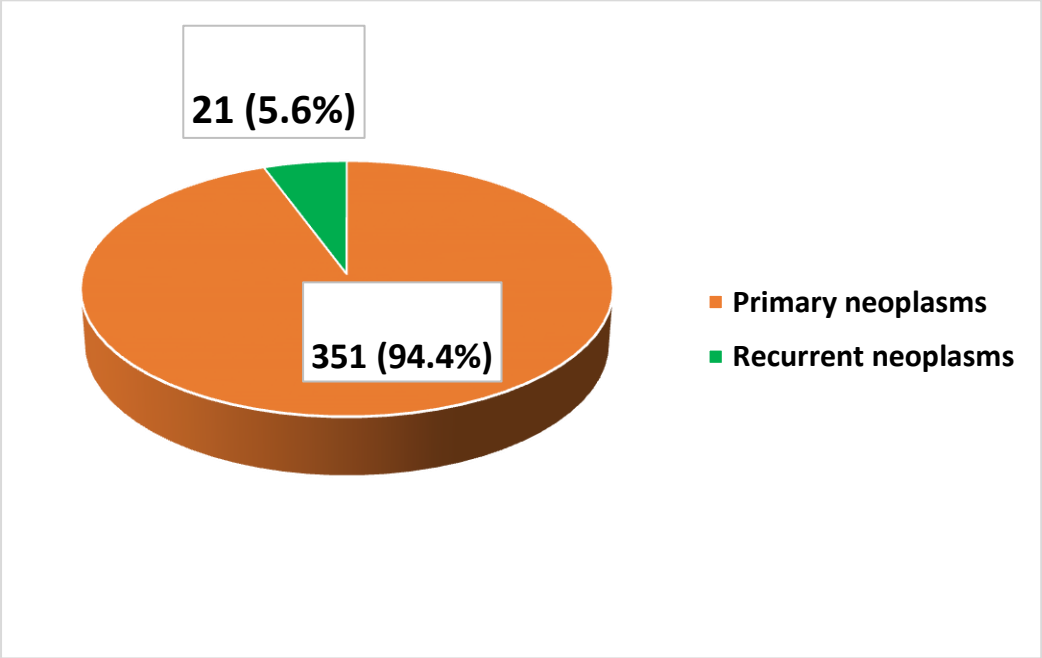

Figure 4: Pattern of occurrence of ONs

3.3.1 Pattern of occurrence of ONs in relation to gender

Table 2 presents comparison between occurrence of ONs and gender of patients.

Table 2: Comparison between the gender of the patient and occurrence of ONs

		Occurrence of the ONs			
		Recurrent Neoplasm		Primary Neoplasm	
		N	%	n	%
Sex	Male	8	4.7%	162	95.3%
	Female	13	6.4%	189	93.6%
	Total	**21**	**5.6%**	**351**	**94.4%**

Notes. Pearson Chi-Square (χ^2) = 0.519, *p*-value = 0.471

As indicated, regarding the recurrent neoplasms, the most affected were females (61.9%) while males comprised 38.1%. Likewise, as regards primary neoplasms, the females were 53.8% while the males 46.2%. However, there was no statistically significant association between gender and occurrence of primary or recurrent neoplasms (χ^2 = 0.519, *p*-value > 0.05)

3.3.2 Occurrence of ONs and age group

Regarding the age group of patients, the 20 to 29-year-olds age group had the highest number of primary neoplasms (95 cases) followed by the 10 to 19-year-olds (81 cases). The 20 to 29-year-olds age group was still the one with the highest cases (9 out of 21) of recurrent neoplasms followed by the 10 to 19-year-olds and the 30 to 39-year-olds each accounting for 3 cases. These results are illustrated in Figure 5.

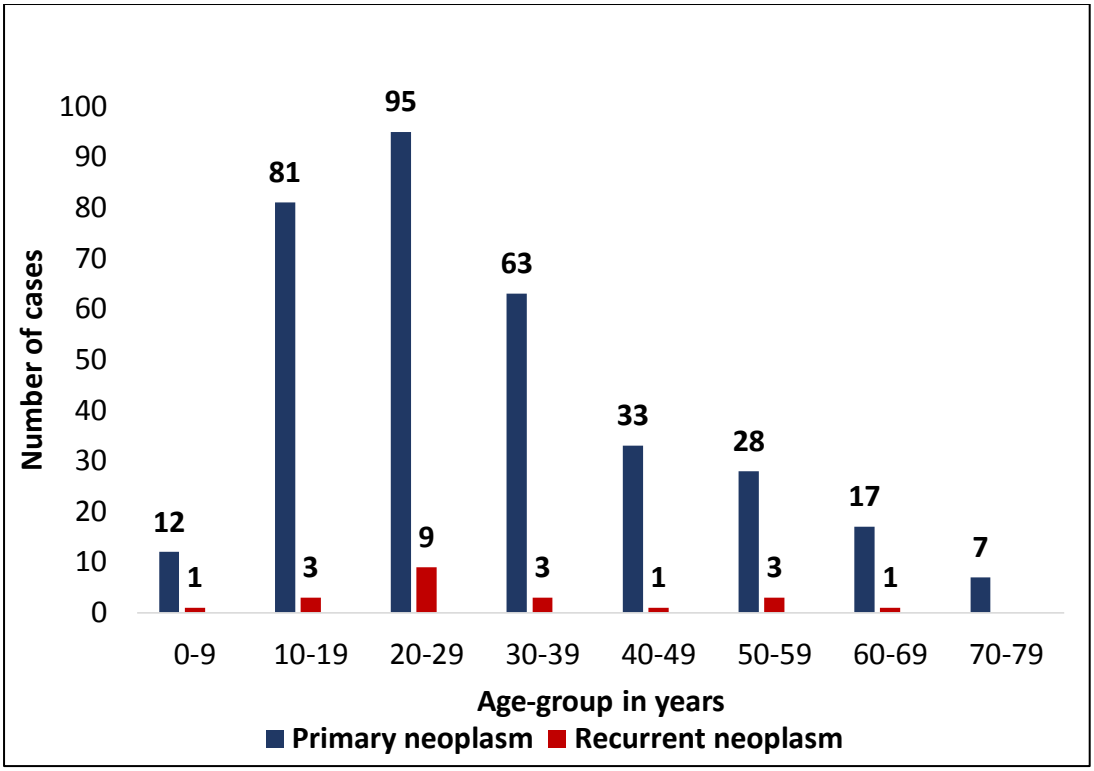

Figure 5: The distribution of ONs according to age groups

3.3.3 Occurrence of ONs and location of residence (rural versus urban)

Table 3 presents the results of comparison between the pattern of occurrence of ONs and patients' area of residence. As indicated, 58.1% of cases with primary neoplasms were from rural areas.

Table 3: The occurrence of ONs and location of residence (rural or urban)

		The occurrence of the ONs			
		Recurrent Neoplasm		Primary Neoplasm	
		n	%	N	%
Home Area	Rural	10	4.4%	216	95.6%
	Urban	11	7.9%	129	92.1%
	Unspecified	0	0.0%	6	100.0%
	Total	**21**	**5.6%**	**351**	**94.4%**

Notes: Pearson Chi-Square (χ^2) = 2.277, *p*-value = 0.320

The Pearson Chi-Square was computed to establish whether there was an association between the home area and the occurrence of ONs. As Table 3 shows, there was no statistically significant association between the occurrence of primary or recurrent ONs and area of residence (χ^2 = 2.277, *p*-value > 0.05).

3.4 Anatomical site of ONs

Majority of ONs (79.3%) were located in the mandible while 19.9% were found in the maxilla. Only 0.8% were located on both mandible and maxilla (see figure 6). The mandible to maxilla ratio was approximately 4:1.

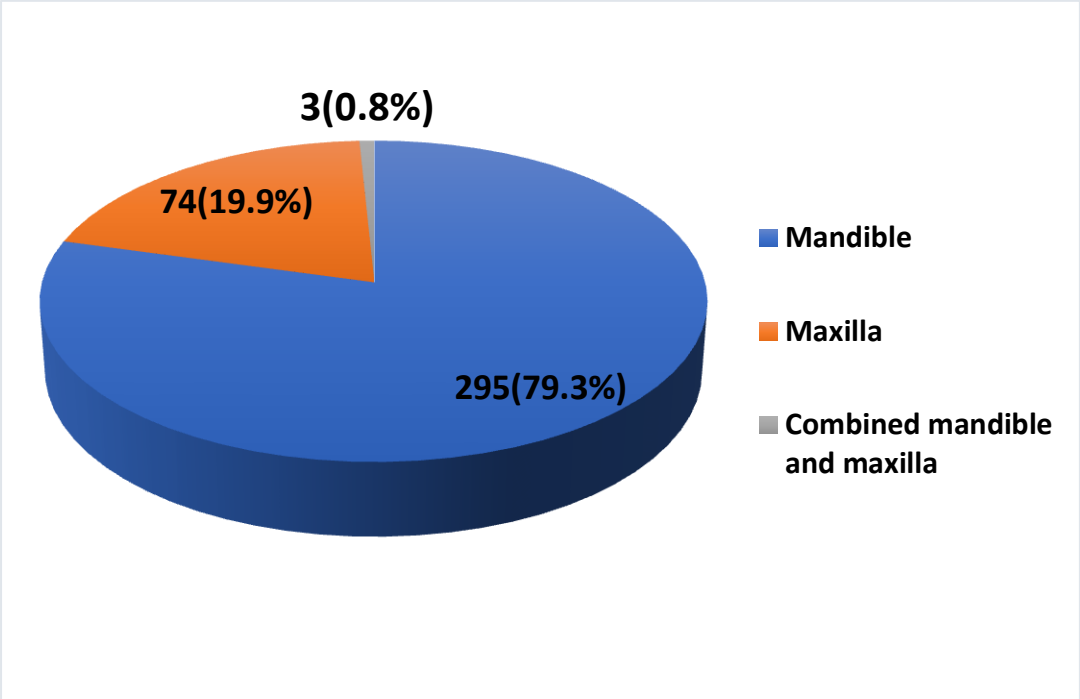

Figure 6: Distribution of ONs in the jaws

Figure 7 illustrates the specific anatomical sites where ONs occurred. Regarding the location of the lesions, 50.0% were found in the posterior mandible while 18.5% were in the anterior mandible. 11.0% were located in the anterior maxilla. The posterior mandible was the most commonly reported site while the anterior location was the most commonly affected site in the maxilla. Some lesions involved both the maxilla and the mandible. There were 10.8% cases involving both the anterior and posterior mandible while 2.2% were located in both the anterior and posterior maxilla.

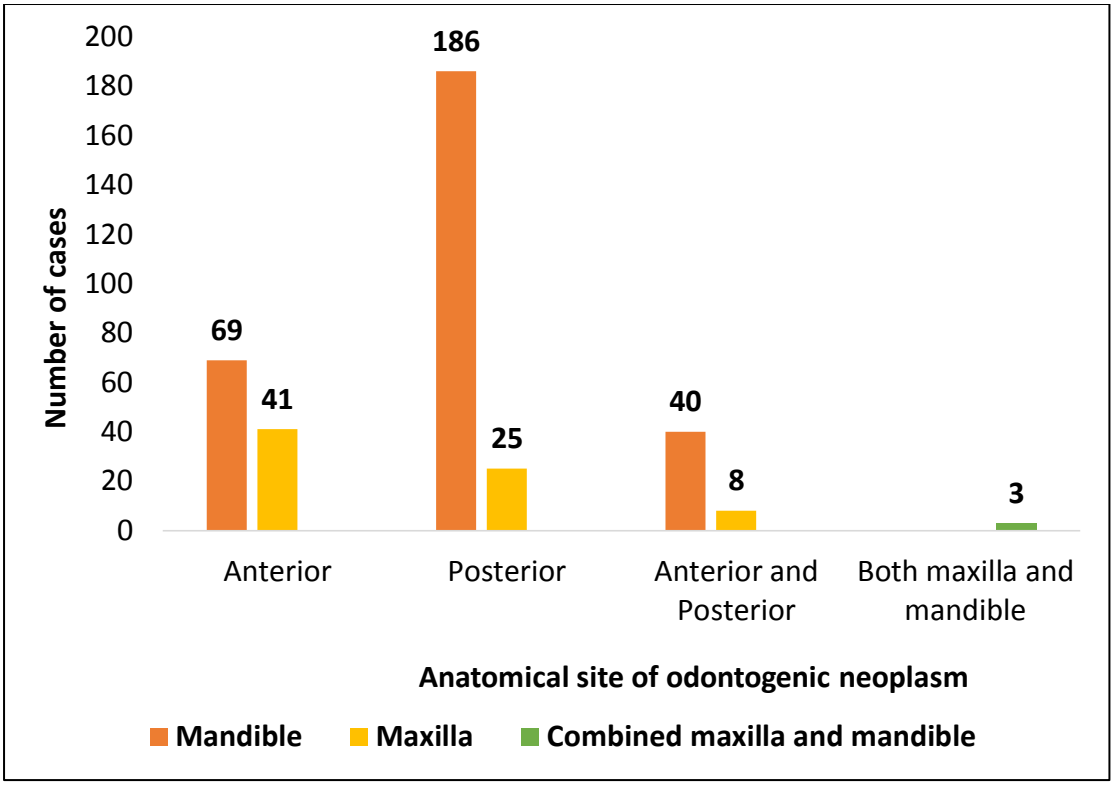

Figure 7: Distribution of ONs according to the anatomical site

3.4.1 Relationships between anatomical site and demographic characteristics

Pearson's Chi-square was computed to test the association between anatomical site and demographic characteristics of patients with ONs. The results are presented in table 4.

Table 3: Comparison between anatomical site and demographic characteristics

Crosstabs	Pearson Chi-Square	Df	Asymp. Sig. (2-sided)
Gender*Anatomical Site	0.241	2	.887
Home Area*Anatomical Site	1.631	4	.803
Age Group*Anatomical Site	28.054	14	**.014**

Note. N of Valid Cases 372

As indicated, there were no statistically significant relationships between gender and anatomical site (χ^2 = 0.241, *p* value > 0.05) and between home area and anatomical site (χ^2 = 1.631, *p* value > 0.05). However, there was a statistically significant association between age group and the anatomical site of the disease (χ^2 = 28.054, *p* value < 0.05).

3.5 Symptoms at presentation

Figure 8 illustrates the symptoms of ONs at presentation.

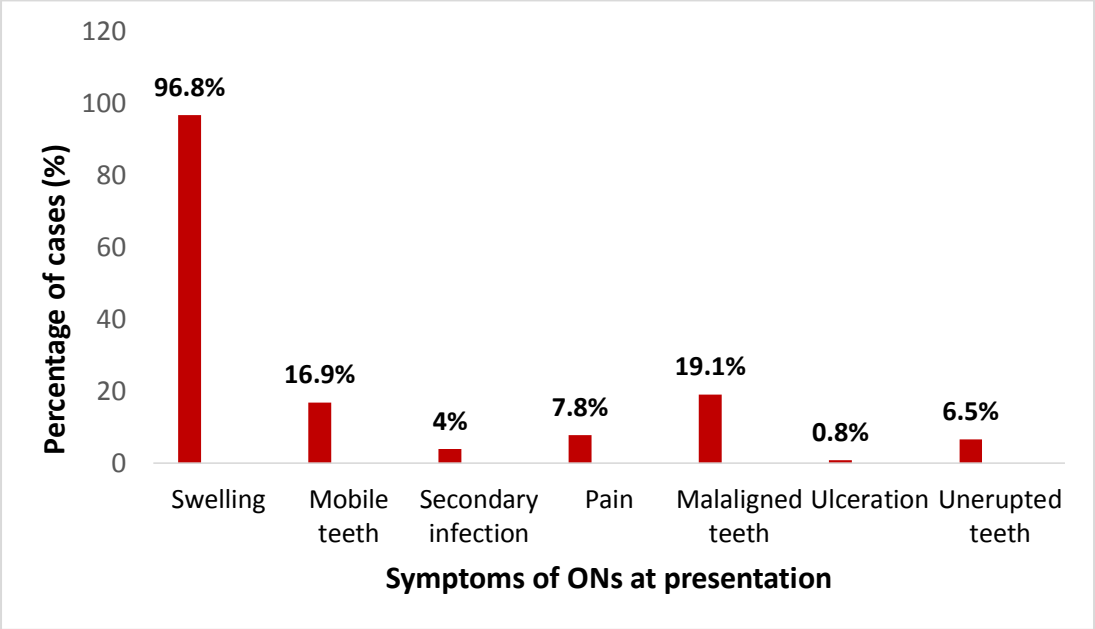

Figure 8. Pattern of symptoms associated with ONs

As indicated in figure 8, swelling was the most commonly reported symptom in 360 cases (96.8%). Mobile teeth were recorded as a symptom in only 63 cases (16.9%). Other reported associated symptoms included secondary infection, pain, mal-aligned/displaced teeth, ulceration and unerupted teeth which were recorded in 15 (4.0%), 29 (7.8%), 71 (19.1%), 3 (0.8%), and 24 (6.5%) of all cases respectively.

3.6 Duration of symptoms at presentation

Results of the duration of symptoms at presentation are illustrated in figure 9. The longest duration of symptoms at presentation was 1 year reported in 19.6% of the cases followed by 2 years recorded in 18.3% of the cases. Duration of less than 1 year was reported in 18.0% of the cases and 3 years in 13.4% of the cases. The duration of the above 10 years was reported in 4.6% of cases. Notwithstanding, there were 1.1% of cases whose durations were not specified.

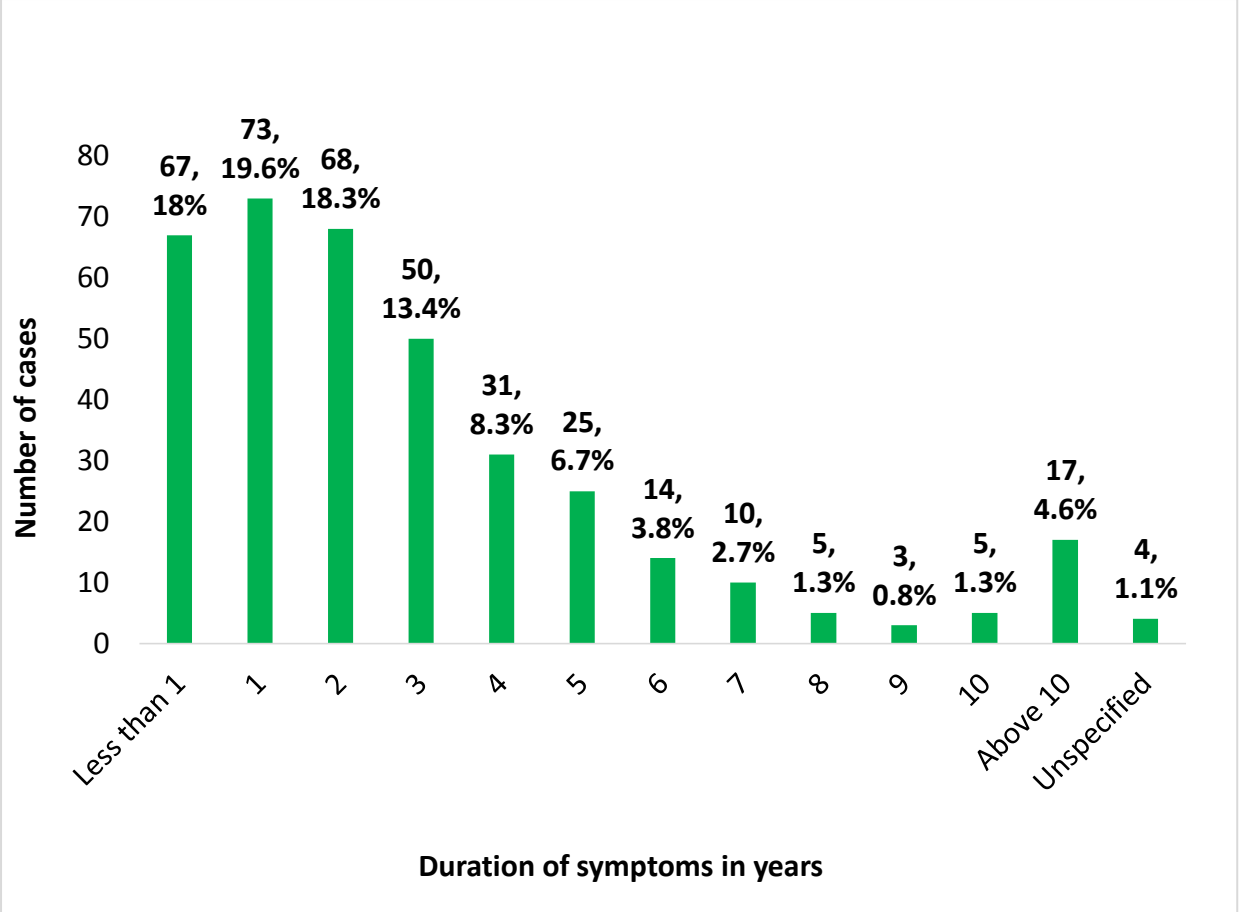

Figure 9: Duration of symptoms associated with ONs at presentation

3.7 Histological diagnoses

Histological diagnoses demonstrated in figure 10 revealed that majority were ONs of epithelial origin that included 242 (65.1%) cases of ameloblastoma and 17 (4.6%) cases of adenomatoid odontogenic tumour. ONs of mesenchymal origin were cemento-ossifying fibroma, odontogenic myxoma (OM) and odontogenic fibroma that accounted for 40 (10.8%), 35 (9.4%), and 4 (1.1%) cases respectively. ONs of mixed origin were odontoma and ameloblastic fibroma with each accounting for 27 (7.3%) and 4 (1.1%) cases respectively. Malignant ONs were of epithelial origin and included clear cell odontogenic carcinoma (CCOC) and ameloblastic carcinoma (AC) with 2 cases and 1 case respectively.

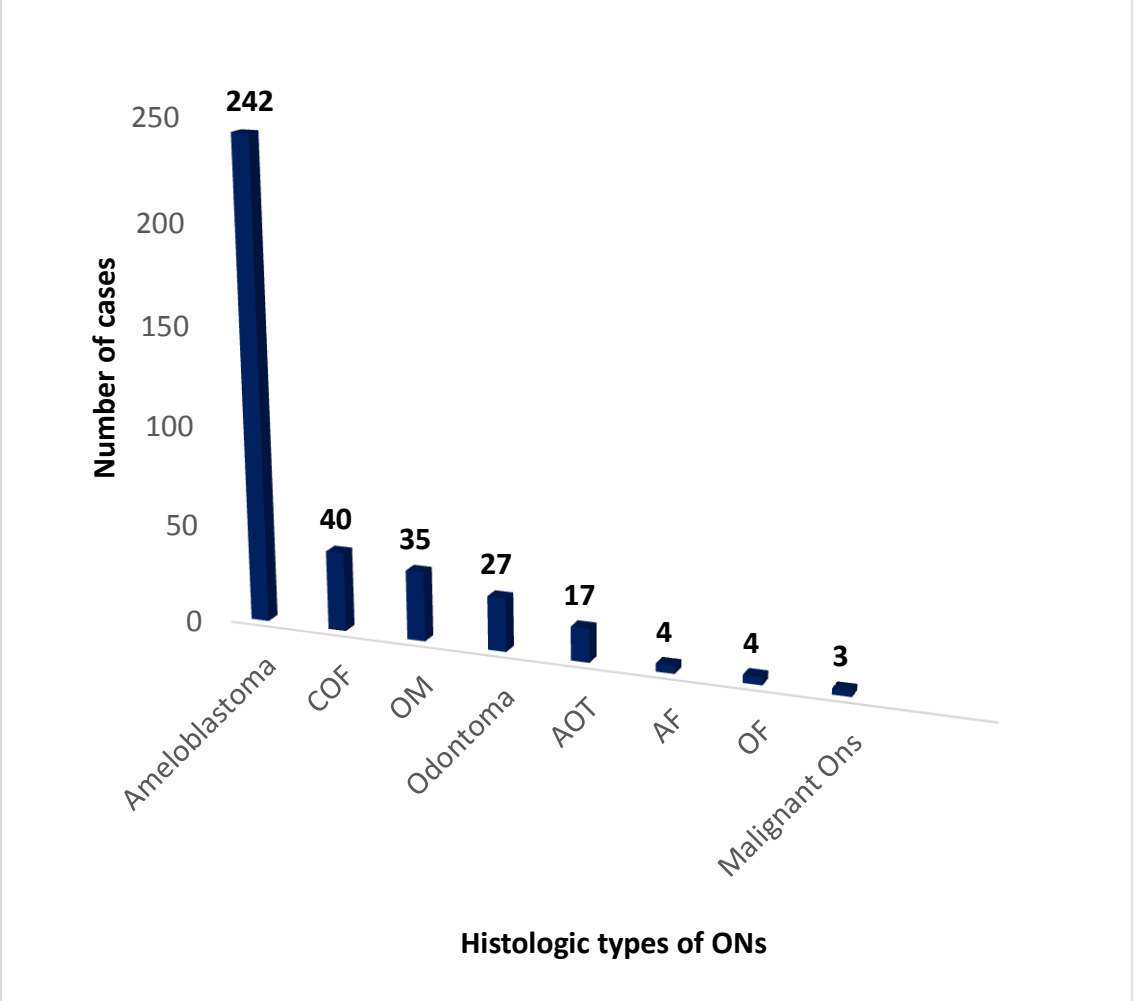

Figure 10: Histological diagnoses of the various ONs that presented at the KNH and the UNDH

3.8 Histological sub-types

The histological subtypes for the majority 197 (53.0%) of the cases of ONs were unspecified (see table 5). With regard to the known histological subtypes of ameloblastoma, 13.7% were of the follicular type followed by those that were of plexiform pattern (11.8%). Cystic histological subtype was in 11.3% of cases. With regard to mixed histological subtypes, follicular and cystic were the highest cases (n =13, 3.5%). Only 2 (0.5%) cases of odontoma were recorded as complex histological subtypes.

Table 5: Distribution of histological subtypes of ONs

	Frequency	Percent
Ameloblastoma		
Plexiform	44	11.8
Cystic	42	11.3
Follicular	51	13.7
Granular	1	0.3
Mixed		
Plexiform and desmoplastic	2	0.5
Follicular and cystic	13	3.5
Follicular and plexiform and cystic	12	3.2
Plexiform and cystic	6	1.6
Plexiform and follicular	2	0.5
Unspecified	69	18.5
Odontoma		
Complex	2	0.5
Unspecified	25	6.7
Others unspecified	103	27.7
Total	**372**	**100.0**

Notes: Pearson Chi-Square (χ^2) = 175.00, *p*-value = 0.000

3.8.1 Comparison between histological diagnosis and histological subtypes

As indicated in table 5, only ameloblastoma and odontoma had histological subtypes that were observed and recorded. Out of the 372 cases, 197 cases did not have specified histological subtypes. Ameloblastoma had the majority of specified histological sub-types. With regard to recorded histological subtypes of ameloblastoma, majority (51) of the cases recorded were follicular in nature followed by those that were plexiform. Forty-two (42) cases of cystic histological subtype were recorded in ameloblastoma diagnosis. The granular histological subtype was rare among the ameloblastomas with only 1 case was reported. With regard to odontoma, 2 cases were recorded as having had a complex histological subtype. In addition, the association between histological diagnosis and histological subtype was found to have been statistically significant (χ^2 = 175.00, *p* value < 0.05).

3.9 Pattern of specific ONs

This section presents the patterns of specific odontogenic neoplasms. These neoplasms include *ameloblastoma, cemento-ossifying fibroma, adenomatoid odontogenic tumour, odontogenic myxoma (fibromyxoma), odontoma, odontogenic fibroma, ameloblastic fibroma, clear cell odontogenic carcinoma, and ameloblastic carcinoma.*

3.9.1 Histological diagnosis in terms of gender

Table 6 illustrates the results of each histological diagnosis in terms of patients' gender.

a. Ameloblastoma

Ameloblastoma was the most reported histological diagnosis in KNH and UNDH in the last 7 years. With regard to gender, the most affected 122 (50.4%) cases were females. However, there was difference of 2 cases of ameloblastomas between the male and female.

b. Cemento-ossifying fibroma

As indicated in table 6, majority 23 (57.5%) of the reported cases were female. This diagnosis was the second most reported (40 cases) in both genders after ameloblastoma.

Table 4: Histological diagnoses in relation to gender

	Male	Female	Total
Histological Diagnosis	Count	Count	Count
Cemento-ossifying Fibroma	17 (42.5%)	23 (57.5%)	40
Ameloblastoma	120 (49.6%	122 (50.4%)	242
Adenomatoid odontogenic tumour	5 (29.4%)	12 (70.6%)	17
Clear cell odontogenic carcinoma	-	2 (100%)	2
Odontogenic myxoma (fibromyxoma)	13 (37.1%)	22 (62.8%)	35
Odontoma	12 (44.4%)	15 (55.6%)	27
Odontogenic fibroma	-	4 (100%)	4
Ameloblastic fibroma	2 (50%)	2 (50%)	4
Ameloblastic carcinoma	-	1(100%)	1
Total	**170**	**202**	**372**

c. Odontogenic myxoma

This was the third most reported histological diagnosis and accounted for 35 cases. Like the rest, majority (62.8%) recorded cases were females.

d. Odontoma

This histological diagnosis was fourth in terms of the number of cases reported over 7 years. The number of affected female cases 15 (55.6%) were more than the male ones 12 (44.4%).

e. Adenomatoid odontogenic tumour

This histological diagnosis was fifth in terms of the total number of reported cases. The majority 12 (70.6%) of the affected cases were females.

f. Odontogenic fibroma and ameloblastic fibroma

These histological diagnoses were sixth in terms of the total number of reported cases. There were 4 cases reported in each. However, there were no male cases reported in odontogenic fibroma. In addition, there were equal numbers of male and female cases in ameloblastic Fibroma.

g. Clear cell odontogenic carcinoma and ameloblastic carcinoma

These histological diagnoses were reported in 3 cases. All the cases were females.

3.9.2. Association between gender and histological diagnosis

The association between gender and histological was not statistically significant (χ^2= 9.240, *p*-value > 0.05).

3.9.3 Histological diagnoses in terms of age group

Table 7 illustrates the results of the analysis of histological diagnoses in terms of age group.

Table 7: Histological Diagnoses in Terms of Age Group

Histological Diagnosis		Frequency	Percent
Cemento-ossifying fibroma	1 to 9 years	2	5.0
	10 to 19 years	13	32.5
	20 to 29 years	7	17.5
	30 to 39 years	7	17.5
	40 to 49 years	8	20.0
	50 to 59 years	1	2.5
	70 to 79 years	1	2.5
	Specified adult	1	2.5
	Total	**40**	**100.0**
Ameloblastoma	1 to 9 years	3	1.2
	10 to 19 years	40	16.5
	20 to 29 years	76	31.4
	30 to 39 years	50	20.7
	40 to 49 years	23	9.5
	50 to 59 years	24	9.9
	60 to 69 years	14	5.8
	70 to 79 years	4	1.7
	Specified adult	8	3.3
	Total	**242**	**100.0**
Adenomatoid odontogenic tumour	10 to 19 years	5	29.4
	20 to 29 years	4	23.5
	30 to 39 years	3	17.6
	40 to 49 years	1	5.9
	50 to 59 years	2	11.8
	60 to 69 years	1	5.9
	Specified adult	1	5.9
	Total	**17**	**100.0**
Clear cell odontogenic carcinoma	50 to 59 years	1	50.0
	70 to 79 years	1	100.0
	Total	**2**	**100.0**
Ameloblastic carcinoma	**Specified as adult**	**1**	**100.0**
Odontogenic myxoma	1 to 9 years	1	2.9
	10 to 19 years	11	31.4
	20 to 29 years	13	37.1
	30 to 39 years	4	11.4
	50 to 59 years	2	5.7
	60 to 69 years	2	5.7
	Specified adult	2	5.7
	Total	**35**	**100.0**

Odontoma	1 to 9 years	7	25.9
	10 to 19 years	12	44.4
	20 to 29 years	3	11.1
	30 to 39 years	1	3.7
	40 to 49 years	2	7.4
	70 to 79 years	1	3.7
	Specified adult	1	3.7
	Total	**27**	**100.0**
Odontogenic fibroma	30 to 39 years	1	25.0
	50 to 59 years	1	25.0
	60 to 69 years	1	25.0
	Specified adult	1	25.0
	Total	**4**	**100.0**
Ameloblastic Fibroma	10 to 19 years	3	75.0
	20 to 29 years	1	25.0
	Total	**4**	**100.0**

Table 7: Histological Diagnoses in Terms of Age Group

As shown, there were more cases of cemento-ossifying fibroma in patients whose age ranged from 1 to 39 years. In addition, ameloblastoma was common in patients whose ages ranged from 1 to 39 years. AOT was reported in most 12 cases in patients aged between 1 to 39 years. However, the association between age group and histological diagnosis was statistically significant (χ^2= 16.672, *p*-value < 0.05).

3.9.4 Histological diagnoses in terms of location of residence (urban or rural)

Table 8 presents the results of the analysis of the histological diagnoses in terms of home area

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Table 8: Histological diagnoses in terms of location of residence

	Location of residence			
	Rural	Urban	Unspecified	Total
Histological diagnosis	Count	Count	Count	Count
Cemento-ossifying fibroma	27	13	-	40
Ameloblastoma	148	89	5	242
Adenomatoid odontogenic tumour	7	10	-	17
Clear cell odontogenic carcinoma	2	-	-	2
Odontogenic myxoma (Fibromyxoma)	29	5	1	35
Odontoma	9	18	-	27
Odontogenic fibroma	2	2	-	4
Ameloblastic fibroma	2	2	-	4
Ameloblastic carcinoma	1	-	-	1
Total	**226**	**140**	**6**	**372**

Notes: Pearson Chi-Square (χ^2) = 47.758, *p*-value = 0.000

As indicated in table 8 there were more cases (67.5%) of cemento-ossifying fibroma in patients whose areas of residence were in rural areas. With regard to ameloblastoma, majority (61.2%) of the cases recorded were from rural areas. However, the adenomatoid odontogenic tumour was common in patients living in urban areas. Clear cell odontogenic carcinoma and ameloblastic carcinoma were rare with origin of cases from rural areas. Odontogenic myxoma was found to be common to patients from rural areas. Nonetheless, odontoma was common to patients from urban areas. The association between histological diagnosis and home area was found to be statistically significant (χ^2= 47.758, *p*-value < 0.05).

3.9.5 Histological diagnoses in terms of occurrence

Table 9 exhibits the results of the analysis of histological diagnoses in terms of occurrence (whether primary neoplasm or recurrent neoplasm). All reported cases of cemento-ossifying fibroma, clear cell odontogenic carcinoma, ameloblastic carcinoma, odontogenic myxoma, odontoma, odontogenic fibroma, ameloblastic fibroma were primary neoplasms. However, in all the reported cases of ameloblastoma, 92.1% were primary neoplasms while 7.9% were recurrent neoplasms. Likewise, there were more cases (88.2%) of primary neoplasms reported of the adenomatoid odontogenic tumour than recurrent neoplasms. However, the association between occurrence of ONs and histological diagnosis was not statistically significant (χ^2= 10.167, *p*-value > 0.05).

Table 9: Histological diagnoses in terms of occurrence of the ONs

	Occurrence of the ONs		
	Recurrent Neoplasm	Primary Neoplasm	Total
Histological Diagnosis	Count	Count	Count
Cemento-ossifying Fibroma	-	40	40
Ameloblastoma	19	223	242
Adenomatoid odontogenic tumour	2	15	17
Clear cell odontogenic carcinoma	-	2	3
Odontogenic myxoma	-	35	35
Odontoma	-	27	27
Odontogenic fibroma	-	4	4
Ameloblastic fibroma	-	4	4
Ameloblastic carcinoma	-	1	1
Total	**21**	**351**	**372**

Notes: Pearson Chi-Square (χ^2) = 10.167, *p*-value = 0.253

3.9.6 Histological diagnoses in terms of anatomical sites

Table 10 presents the results of the analysis of histological diagnoses in terms of the anatomical site. There were more cases of cemento-ossifying fibroma in the mandible than in the maxilla. With regard to ameloblastoma, majority (93.4%) were found in the mandible. The adenomatoid odontogenic tumour was common in the mandible as well as clear cell odontogenic carcinoma. Odontogenic myxoma was common in the mandible. However, odontoma was common in the maxilla. Odontogenic fibroma and ameloblastic fibroma were common in the mandible. Only cemento-ossifying fibroma and ameloblastoma occurred in the mandible and maxilla in the same patient respectively. The association between anatomical site and histological diagnosis was statistically significant (χ^2= 109.190, *p*-value < 0.05).

Table 10: Histological diagnoses in relation to anatomical site

	Anatomical site(s)			
	Mandible	Maxilla	Combined mandible and maxilla	Total
Histological Diagnosis	Count	Count	Count	Count
Cemento-ossifying Fibroma	18	21	1	40
Ameloblastoma	226	14	2	242
Adenomatoid Odontogenic Tumor	12	5	-	17
Clear Cell Odontogenic Carcinoma	2	-	-	3
Myxoma (Odontogenic Myxoma)	20	12	-	32
Odontema	9	18	-	27
Odontogenic fibroma	3	1	-	4
Ameloblastic Fibroma	4	-	-	4
Ameloblastic carcinoma	1	-	-	1
Total	**295**	**74**	**3**	**372**

Notes: Pearson Chi-Square (χ^2) = 109.190, *p*-value = 0.000

3.9.7 Histological diagnoses in terms of symptoms at presentation

Results of the analysis of histological diagnoses and symptoms at presentation are presented in table 11.

Table 11: Histological diagnoses in terms of symptoms

	Swelling	Mobile Teeth	Infection	Pain	Malaligned Teeth	Ulceration	Unerupted Teeth
Histological Diagnosis	Count	Count	Count	Count	Count	Count	Count
1. Cemento-ossifying fibroma	40	-	-	1	-	-	2
2. Ameloblastoma	242	50	10	25	50	1	2
3. Adenomatoid odontogenic tumor	17	1	1	-	-	-	-
4. Clear Cell Odontogenic Carcinoma	2	-	1	-	1	1	-
5. Odontogenic myxoma	35	4	1	1	10	-	-
6. Odontoma	15	5	2	1	10	-	20
7. Odontogenic fibroma	4	1	-	-	-	-	-
8. Ameloblastic fibroma	4	2	-	-	-	-	-
9. Ameloblastic carcinoma	1	-	-	1	-	1	-

Notes: Pearson Chi-Square (χ^2) = 66.324, df = 48, *p*-value = 0.041

As shown in table 11, majority of the ONs (97%) were manifested as swellings. In addition, all the diagnoses presented with more than one symptom. There were a considerable number of ameloblastomas that presented with mobile and mal-aligned/displaced teeth. However, the association between symptoms at presentation and histological diagnosis was statistically significant (χ^2= 66.324, *p*-value < 0.05).

3.9.8 Histological diagnoses in terms of duration of symptoms

Table 12 shows the results of the analysis of histological diagnoses in terms of duration of symptoms.

Table 12: Histological diagnoses in terms of duration of symptoms at presentation

	Duration of Symptoms at Presentation					
	Less than 1 year	1 to 5 years	6 to 10 years	Above 10 years	Unspecified	Total
Histological diagnosis	Count	Count	Count	Count	Count	Count
Cemento-ossifying Fibroma	4	31	4	1	-	40
Ameloblastoma	42	159	24	13	4	242
Adenomatoid odontogenic tumour	4	13	-	-	-	17
Clear cell odontogenic carcinoma	1	1	-	-	-	2
Odontogenic myxoma	10	23	1	1	-	35
Odontoma	4	14	7	2	-	27
Odontogenic fibroma	-	4	-	-	-	4
Ameloblastic fibroma	2	1	1	-	-	4
Ameloblastic carcinoma	-	1	-	-	-	1
Total	**67**	**247**	**37**	**17**	**4**	**372**

Notes: Pearson Chi-Square (χ^2) 25.598, df = 24, *p*-value = 0.374

As indicated in table 12, there were more cases of cemento-ossifying fibroma whose duration of symptoms at presentation was between 1 to 5 years. With regard to ameloblastoma, the duration of symptoms in the 159 (65.7%) of the cases ranged from 1 to 5 years. There were 4 cases (1.7%) whose duration of symptoms was unspecified. Likewise, symptoms of majority 13 (76.5%) of the adenomatoid odontogenic tumours ranged from 1 to 5 years. This was the case with myxomas and odontomas. However, the association between the duration of symptoms at presentation and histological diagnosis was not statistically significant (χ^2= 25.598, *p*-value > 0.05).

3.9.9 Histological diagnoses in terms of histological sub-types

Table 13 illustrates the results of the analysis of histological diagnoses in terms of histological subtypes.

Table 13: Histological diagnoses in terms of histological subtype

Histological Diagnosis		Frequency	Percent
Cemento-ossifying fibroma	Unspecified	40	100.0
Ameloblastoma	Plexiform	44	18.2
	Cystic	42	17.4
	Follicular	51	21.1
	Mixed		
	Plexiform and desmoplastic	2	0.8
	Follicular and cystic	13	5.4
	Follicular, plexiform and Cystic	12	5.0
	Plexiform and cystic	6	2.5
	Plexiform and follicular	2	0.8
	Granular	1	0.4
	Unspecified	69	28.5
	Total	**242**	**100.0**
Adenomatoid odontogenic tumour	Unspecified	17	100.0
Clear cell odontogenic carcinoma	Unspecified	2	100.0
Odontogenic myxoma	Unspecified	35	100.0
Odontoma	Complex	2	7.4
	Unspecified	25	92.6
	Total	**27**	**100.0**
Odontogenic fibroma	Unspecified	4	100.0
Ameloblastic fibroma	Unspecified	4	100.0
Ameloblastic carcinoma	Unspecified	1	100.0

As shown in table 13, histological sub-types were unspecified in cemento-ossifying fibroma, adenomatoid odontogenic tumours, clear cell odontogenic carcinoma, ameloblastic carcinoma, odontogenic myxoma, odontogenic fibroma, ameloblastic fibroma cases. However, ameloblastoma cases were presented as many histological sub-types among which the majority 51 (21.1%) were follicular type. Moreover, there were 69 cases of ameloblastoma whose histological subtypes were undefined. Also, there were 2 odontoma (0.5%) cases whose histological subtypes were complex. However, the association between histological subtype and histological diagnosis was not statistically significant (χ^2= 175.00, *p*-value < 0.05).

CHAPTER FOUR

DISCUSSION

4.1 Socio-demographic pattern

Odontogenic neoplasms are common jaw lesions in the sub-Sahara Africa region [13,15,16]. A of total of 782 case records were examined in this study among which 372 (47.6%) cases were ONs. This finding corroborates with that of a Kenyan study by Butt et al. in 2012 (69.85%) and a Nigerian study by Lawal et al in 2013 (41.7%) [13,15]. In this study, there were 26.1% cases of the ONs in the first two decades of life which was a lower proportion when compared to a study at the University of Limpopo by Mamabulo et al. (2011) that had 32.7% cases of ONs involving patients in the same age group [17].

The female to male ratio in this study was 1.1:1. However, this difference was not statistically significant. A previous Kenyan study also showed no gender predilection [13]. Various other studies in different countries have shown a predilection of the male gender [14,15,18,19]. However, De Medeiros et al. (Brazil, 2018) showed a female predilection [20].

The age-range observed in this study was 5.5-78 years. The male age-range was 5.5-77 years while that of females was 8-76 years. The variation in the age-range among the genders was not statistically significant. These findings are comparable to those of Butt et al. in 2012 (5-85 years) and De Medeiros et al. in 2018 (5-81 years) [13,20]. Nalabolu et al. (2017) and Lawal et al. (2013) showed involvement in lower ages of 1-70 years and 3-82 years respectively [16, 18].

The peak of ONs in this study is the third decade of life. The majority of the cases were below 40 years of age (54.1%) with most cases in the second, third and fourth decades of life. Butt et al. (2012) showed the peak to have been 11-50 years which differs slightly in the current trend [13]. Lawal et al. (2013) showed a peak in the third decade as well while Nalabolu et al. (2017) found the third and fourth decades to have been the peak ages [15,18].

ONs presented were mostly of patients who reside in rural areas (226 cases, 60.8%). However, there was no association in the general pattern of ONs in relation to area of

residence. An Ethiopian study by Kebede et al. (2017) showed a higher rural population (58.9%) in the cases they looked at [14].

4.2. Clinical pattern

The presentation of ONs clinically was varied. They were predominantly benign neoplasms (99.2%) with malignant ONs having been rare (0.8%). This high proportion of benign ONs is in line with other studies in Africa (98.6%) and Brazil (99.2%) [12,15,20]. However, an Ethiopian study shows the malignant ONs were high at 19% [14].

Primary neoplasms were predominant with 351 (94.4%) cases while recurrent neoplasms were 21 (5.6%). The trend in an Italian study by Rubini et al. (2017) was slightly different, showed a higher proportion of recurrent neoplasms (67, 19.5%) as compared to this study, but an overall higher proportion of primary neoplasms (277, 80.5%) [21].

The commonest site for ONs was the mandible with 79.3% of cases, predominantly in the posterior region. In the maxilla, the anterior region was the most commonly involved. The mandible to maxilla ratio was 4:1. Studies from Africa, Asia, Europe, and South America indicate the mandible as the frequent site for ONs [14, 15, 16, 18, 20,21, 22, 23]. Nalabolu et al. (2017) recorded a higher number of ONs in the posterior mandible and anterior maxilla as seen in this study [18]. De Medeiros et al. (2018) also recorded the posterior region of the mandible as the commonest site.[20]

Swelling was the most commonly reported symptom. All the ONs expect for 12 cases of odontomas presented as swellings. Other symptoms observed included mobile teeth, unerupted teeth, mal-aligned teeth, pain and ulceration.

4.3. Histological pattern

Histopathological presentations of odontogenic neoplasms are varied across geographical regions. This study demonstrates three histological types of ONs. These were epithelial ONs (262 cases, 71%), mixed ONs (79 cases, 21%) and mesenchymal ONs (31 cases, 8%). A Brazilian study corroborates these findings [20]. However, a

Kenyan study by Butt et al. (2012) had reported a slightly different trend with the mesenchymal types presenting more than the mixed types [13].

Among benign ONs, the most common epithelial types included ameloblastoma and adenomatoid odontogenic tumour. The mixed types were odontomas, ameloblastic fibroma. The mesenchymal types included were cemento-ossifying fibroma, odontogenic myxoma and odontogenic fibroma. The malignant ONs were epithelial in origin and included clear cell odontogenic carcinoma and ameloblastic carcinoma.

The common ON is the ameloblastoma (242 cases, 65.1%). This is similar to studies done across the world. [13-21] This was followed by cemento-ossifying fibroma, odontogenic myxoma, odontoma, adenomatoid odontogenic tumour, odontogenic fibroma, and ameloblastic fibroma in a decreasing manner. However, these findings differ with Noureldin et al. (2019) who showed the odontoma (34.62%) as the most common followed by ameloblastoma (15.38%) [22]. The malignant ONs included two clear cell odontogenic carcinoma and one ameloblastic carcinoma. These histologic types vary across several studies but are commonly featured [13-21].

The ameloblastoma and odontoma manifested in various histological forms. The most common histologic subtype of ameloblastoma was the follicular type. The other subtypes included plexiform, cystic and mixed patterns. The granular pattern was very rare having been reported in only one case. Saghravanian et al. (2016) found the plexiform type as the commonest histologic subtype of ameloblastoma followed by follicular and mixed types [24]. Intapa et al. in 2017 also found the plexiform subtype to have been the most common followed by the follicular and the acanthomatous subtypes [25]. In the case of odontoma only two cases were reported as the complex subtype while the other cases were not specified.

CONCLUSIONS

1. ONs are common among patients presenting with jaw lesions at the KNH and the UNDH
2. Patients below 40 years were mostly affected thus need for high index of suspicion in patients in this age-group presenting with jaw lesions.
3. There was no gender predilection in the pattern of occurrence of ONs.
4. The mandible was the most involved site with ONs predominantly occurring in the posterior region.
5. Ameloblastoma is the most commonly occurring ON with the follicular subtype being predominant.
6. Most of the patients presented late with symptoms having been experienced for more than 1 year.

RECOMMENDATIONS

1. Identification of the histologic subtype in ameloblastoma cases must be done as it has a bearing on aggressiveness of the neoplasm and the extent of surgical management.
2. Promotion of specialised medical services closer to the people such as in rural areas where a majority of the Kenyan population reside through the creation and implementation of policies in the public health system that will impact on the diagnosis and management of ONs by:
    a. Training relevant personnel e.g. oral and maxillofacial surgeons, oral pathologists and technologists.
    b. Setting up of theatre facilities in regional hospitals in the country/allocating more theatre space for the management of odontogenic neoplasms.
    c. Provision of imaging services and reconstruction implants through universal health coverage so as to enable prompt intervention, especially to the resource-limited citizenry.
3. Sensitization of the citizenry on the occurrence of odontogenic neoplasms, the long-term effects and the need to seek early treatment (less than 1year since the onset of symptoms)

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APPENDICES

Appendix I: Data Collection Tool

UNIVERSITY OF NAIROBI

School of Dental Sciences

Study Topic: CLINICO-PATHOLOGICAL PATTERN OF ODONTOGENIC NEOPLASMS AT TWO NATIONAL REFERRAL CENTRES IN NAIROBI, KENYA

1. Age of the patient: Age:_____
2. Gender of the patient: ☐ Male ☐ Female
3. Home area: ☐ Rural ☐ Urban
4. Nationality: _____
5. Primary neoplasm: _____
6. Recurrent neoplasm: _____
7. Anatomical site of disease: _____
8. Symptoms: _____
   _____
   _____
   _____
9. Duration:_____
   _____
   _____
10. Histological diagnosis: _____
    _____
11. Histological subtype: _____
    _____

Appendix II: 2017 WHO Classification of Odontogenic neoplasms

BENIGN ODONTOGENIC NEOPLASMS

Epithelial neoplasms

Ameloblastoma

- Ameloblastoma, Unicystic type
- Ameloblastoma, Extraosseous/peripheral type
- Metastasizing ameloblastoma

Squamous Odontogenic tumor

Calcifying epithelial odontogenic tumor

Adenomatoid odontogenic tumor

Mixed (epithelial and mesenchymal) neoplasms

Ameloblastic fibroma

Primordial odontogenic tumor

Odontoma

- Odontoma, Compound type
- Odontoma, Complex type

Dentinogenic ghost cell tumor

Mesenchymal neoplasms

Odontogenic fibroma

Odontogenic myxoma/myxofibroma

Cementoblastoma

Cemento-ossifying fibroma

Appendix III: 2017 WHO Classification of Odontogenic neoplasms

MALIGNANT ODONTOGENIC NEOPLASMS

Epithelial neoplasms

- Ameloblastic carcinoma
- Primary intraosseous carcinoma
- Sclerosing odontogenic carcinoma
- Clear cell odontogenic carcinoma
- Ghost cell odontogenic carcinoma

Mixed (epithelial and mesenchymal) neoplasms

- Odontogenic carcinosarcoma

Mesenchymal neoplasms

- Odontogenic sarcoma

Appendix IV: Institutional ethics and research committee approval

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12th July 2019

KENYATTA NATIONAL HOSPITAL * APPROVED 12 JUL 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Dr.Michael M. Kezegule
Reg. No.V60/76139/2014
Dept.of Oral and Maxillofacial Surgery, Oral Pathology and Oral Medicine
School of Dental Sciences
College of Health Sciences
University of Nairobi

Dear Dr. Kezegule

RESEARCH PROPOSAL: CLINICO-PATHOLOGICAL PATTERN OF ODONTOGENIC NEOPLASMS AT TWO NATIONAL REFERRAL CENTRES IN NAIROBI, KENYA (P249/03/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 12th July 2019 – 11th July 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L. CHINDIA
SECRETARY, KNH-UoN ERC

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