INTRODUCTION:

The Derivations of Salivary Tissues.

The salivary gland units begin to form at 6-9 weeks gestation. Embryologically, tissues that form salivary gland units for minor and major salivary glands are derived from oral Ectoderm.

Development of each of salivary gland begins with in-growth of tissue from the oral epithelium. Initially they forming solid nests of cells, and later its differentiation leads to tubule formation, with 2 layers of epithelial cells. These are destined to differentiate into ducts, acini, and myoepithelial cells.

The parotid gland becomes encapsulated later in its embryology. This leads to some lymph nodes to become trapped within the gland. Most of these lymph nodes - 11 on average, are located within the superficial or lateral portion of the gland; and the rest - 2 on average - are in the deep portion. This embryologic difference explains why lymphatic metastases may manifest within the substance of the parotid gland

The Anatomic Salivary Gland Secretory Unit

Salivary gland units are made up of acini and ducts.

- The Acini are highly active cells and contain predominantly serous cells. These cells drain their secretions first into the intercalated duct, followed by the striated duct, and finally into the excretory duct.
- Myo-Epithelial Cells surround the Acini and Intercalated Duct and serve to actively expel secretory products into the ductal system.
- Basal Cells along the salivary gland unit replace damaged or turned-over elements.

THE PAROTID GLAND

The paired Parotid Glands are the largest of the Major Salivary Glands. They are located in a compartment anterior to the ear and are invested by a fascia that suspends the gland from the zygomatic arch. The Parotid Compartment thus contains the Parotid Glands, a complex Nervous Structure of Sensory and Secreto-Motor Nerves, Blood Vessels, and Lymphatic Vessels with Lymph Nodes.

The deep anatomic relationships of the parotid gland is important as tumours may arise from within the deep portion and expand into the adjacent parapharyngeal space and may manifest as intraoral masses. These tumours are termed dumb-bell tumours when they grow between the posterior aspect of the mandibular ramus and the stylomandibular ligament; the tumours expand on either side of this constricted area.

The parotid gland is a large unilobular gland through which the facial nerve passes. No true superficial and deep lobes exist. The term superficial parotidectomy or parotid lobectomy refers only to the surgically created boundary from facial nerve dissection.

Stenson's duct is the conduit that allows salivary flow into the oral cavity. The duct is located approximately 1 cm below the Zygoma as it leaves the gland, and runs horizontally towards the buccal cavity. It passes anteriorly to the masseter muscle and then penetrates the buccinator muscle to open intraorally opposite the second maxillary molar.

Branches of the External Carotid Artery provide arterial supply to the parotid gland. The Posterior Facial Vein provides venous drainage, and lymphatic drainage is from lymph nodes within and external to the gland that leads on to the Deep Jugular Lymphatic Chain.

The gland receives Parasympathetic Secretomotor Innervation from preganglionic fibres that arise in the Inferior Salivatory Nucleus. These fibres travel with the Glossopharyngeal Nerve to exit the skull base via the Jugular Foramen. The postganglionic fibres travel with the Auriculo-Temporal Nerve to supply the parotid gland

LITERATURE REVIEW

Salivary Gland Tumours account for 3% of all Head and Neck Tumours; and approximately 0.6% of all neoplasms.

Some 70% to 80% of all Salivary Gland Tumours arise from the Parotid Gland. Approximately 80% of parotid masses are benign neoplasm's [(1).]

Their diagnosis and management are an ongoing surgical challenge. Numerous pathologic processes on the parotid gland are recognized by palpation, which provides a good orientation during clinical examination [(2).]

For a more precise assessment of the pathologic processes, the clinical findings may need to be combined with computed tomography, sialography, ultrasonography and cytology or histology.

AETIOLOGY FOR SALIVARY TUMORIGENESIS:

- At least **two theories** of tumorigenesis have been proposed for salivary gland neoplasm's:
    1. In the Multicellular Theory, each type of neoplasm is thought to originate from a distinctive cell type within the salivary gland unit. This theory is supported by the observation that all differentiated salivary cell types retain the ability to undergo mitosis and to regenerate [(9, 10).]

    2. An alternative theory, the Bicellular Reserve Theory, assumes that the origin of various types of salivary neoplasm's can be traced to the Basal Cells of either the Excretory or Intercalated Duct [(10).]

- The possible reasons for some salivary neoplasm's are also considered to be from genetic and environmental factors, and even nutritionally related conditions.
- Induction of salivary gland tumours following Radiation Therapy for diseases of the head, neck and upper thoracic region has already been reported [(4).]

CLINICAL PRESENTATION:

Patients diagnosed with malignant parotid neoplasm often present with:

- A Mass located in the parotid region,
- Facial Swelling,
- Facial Nerve Dysfunction,
- Pain, and
- Enlarged Lymph Nodes.

Parotid swelling represented 77.3% and 17.4% respectively in studies done in Turkey and Canada; while facial weakness was found in 1.3% and 5.8%. [2, 5].

The three symptoms of pain, facial weakness, and lymph-adenopathy are important clinical indicators of malignancy [5].

TREATMENT MODALITIES:

The standard treatment for most parotid tumours is parotidectomy (partial or total) with sparing of the facial nerve whenever possible.

Radiotherapy is used when a local relapse after surgery is to be expected or for palliation of an inoperable tumour [2].

THE SPECTRUM OF PAROTID NEOPLASMS:

The spectrum of parotid gland neoplasms have been reported extensively in the European and American literature.

Few reports of parotid gland neoplasms have been reported in some parts of Africa [6, 7, 8].

In South Africa, the spectrum of parotid gland neoplasms has been reported in two studies. In a study done in Cape Town, malignant tumours accounted for 31% [4, 11].

CLASSIFICATION:

The histological classification of parotid gland tumours is based on the World Health Organisation's histological Classification of Salivary Gland Tumours, which was established in 1971 and revised in 1991 and 2005. It constitutes a reliable standard for diagnosis and study.

DEMOGRAPHICS:

There appears to be considerable epidemiological differences in different parts of the world. The proportion of malignant tumours in European and American literature is low as demonstrated in Italy (15%), Turkey (17%), United States of America (18%) and Canada (21%).

The proportion of malignant tumours is much higher in African literature and was 44% and 47% in studies conducted in Nigeria and Tanzania respectively. (6, 8).

Parotid gland tumours are classified into benign and malignant tumours. Pleomorphic Adenoma and Warthin's Tumour are the most common benign tumours with different distributions.

Pleomorphic Adenoma represent 83.5%, 65.5%, 51%, and 27% respectively, in studies done in Pakistan, Poland, Taiwan, and Australia, while Warthin's Tumour accounts for 12%, 21%, 23% in Pakistan, Australia and Taiwan. (4, 12, 13, 14).

In a study done in Cape Town; Pleomorphic Adenoma accounted for 42%, while Warthin's tumour represented 8%. (3).

Muco-Epidermoid Carcinoma is the most common parotid malignancy in most studies and accounted for 26%, 30% and 60% respectively in studies done in Australia, Taiwan and Pakistan. (12, 13, 14).

In a Cape Town study, Metastatic Cutaneous Squamous Cell Carcinoma was the most frequent parotid malignancy found - accounting for 22%; Primary Parotid Malignancy represented 16%; and Muco-Epidermoid accounted for 30% of Primary Parotid Malignancy.[3].

Therefore the aim of this study is to retrospectively review the clinical presentation and the histopathology of parotid gland tumours, and to compare the findings with other published studies.

STUDY AIMS AND OBJECTIVES

1. To describe the histopathology of parotid tumours seen in the Division of ORL-HNS at the Academic Hospitals of the University of Witwatersrand.

2. To describe the clinical presentation of these parotid tumours at the Academic Hospitals of the University of Witwatersrand

HYPOTHESIS

This study will show that the proportion of parotid malignant tumours will be comparable to other African studies.

MATERIALS AND METHODS

Study Location

The study was conducted in the clinical units of ORL-HNS at the three University Academic Hospitals; namely: The Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani - Baragwanath Hospital and Helen Joseph Hospital.

Study Period

The fixed study period was 5 years - starting from the 1st January 2006 and ending on the 31st December 2010.

Study Population

The study included all patients that underwent parotid surgery as part of their management for parotid gland tumours; and following on with histopathology analysis of the resected specimen.

Inclusion and Exclusion Criteria

1. For the purposes of this study, only those patients who were identified as patients with parotid gland tumours, on whom parotid surgery was performed, for whom histopathological results were obtained, were included in the final study population and were used for analysis.

2. The following were excluded:

- All patients who had parotid surgery for non neoplastic conditions
- All patients who had parotid surgery outside of the Academic Division of Otorhinolaryngology-Head Neck Surgery
- All patients who had only parotid gland tumour biopsies.

Data Collection

Patients were identified from two sources within each hospital, namely the:

- ENT Operating Room Surgical Register.
- ENT Ward Admission Register.

The Operation Theatre Registers were used as the primary reference to identify patients who were recorded as having had parotid gland surgery as a treatment procedure for parotid gland tumours.

The ENT ward admission registers were used as secondary references to aid in identification of those patients whose information in theatre registers was unclear or lacking in details (e.g. missing or partial hospital numbers, misspelled names).

All of the patients that were clearly identified from the theatre register were recorded as part of initial sample population.

The patient's information was then used to search the database of the National Health Laboratory Services (NHLS) and all findings were recorded into one of the following categories:

1. Histology reports, in which a histological analysis was performed on the specimen
2. No results found, in which no results were found in the database
3. Incomplete or incorrect information, in which patients in the theatre register did not have sufficient information to interrogate the NHLS database.

Patients identified exclusively from the secondary references were cross-checked against their recorded laboratory findings and were included in study population.

The following data were recorded for each patient:

- Age
- Sex
- Presenting symptoms
- Clinical findings
- Date of operation (Specimen collection)
- Histological type

Histological results were obtained from the data available on the NHLS Computer register at each of the hospitals.

All data were recorded electronically using Microsoft Access database and Microsoft Excel spreadsheet.

Data Analysis and Presentation

The following software applications were used for data manipulations, analysis and presentation:

- Microsoft Access database for data storage, retrieval and selection
- Microsoft Excel 2007 spread sheet for descriptive analysis, summary statistics and comparison of sample means
- Web Chi Square Calculator for comparison for sample of populations
- Standard statistical methods were used. Student's *t* test was used to analyse continuous data and the Chi Square (^{X2}) test for ordinal data. A probability (p) value of less than (or equal to) 0.05was regarded as significant.
- Microsoft Word 2007 processor for final documentation and presentation.

ETHICS COMMITTEE APPROVAL FOR STUDY

This conducting of this retrospective study was approved by the Standards and Ethics Committee of the Faculty of Health Sciences of the University of the Witwatersrand.

POTENTIAL LIMITATIONS

- As most retrospective studies, difficulties aroused with collection of data due to poor or lost records.
- Only patients with parotid neoplasm's who underwent definitive surgery were considered.

RESULTS

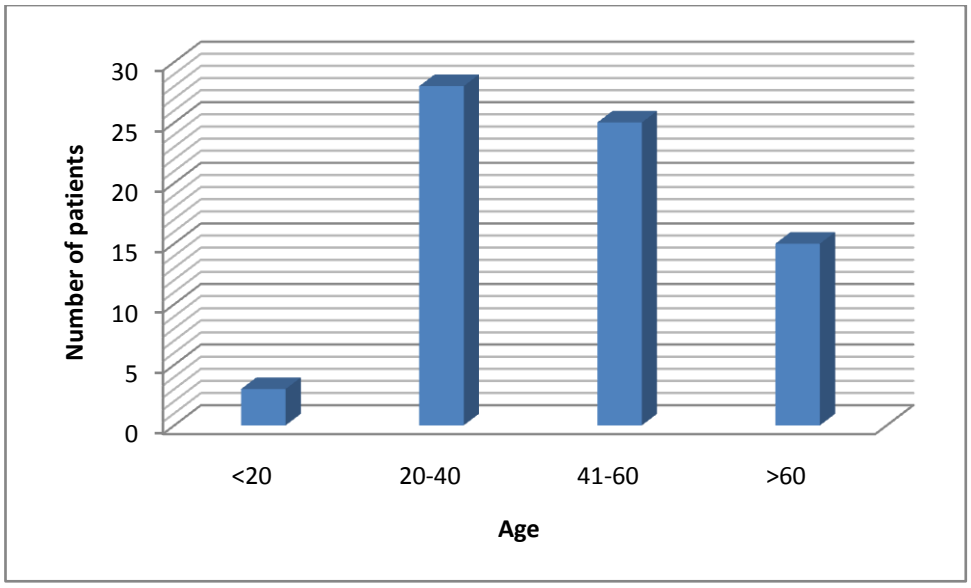
A total of 86 patients were identified from the registers of the operating theatres as patients who have undergone parotid surgery for parotid neoplasms.

The clinical records were incomplete in 15 patients and they were rejected from the study sample and not included in further discussion.

71 patients will be used as the study sample and will be included in further discussion.

Figure 1 **AGE DISTRIBUTION**

The mean age at surgery was 44, the youngest patient was 7 year old and the oldest was 81 year old.



The patients between the age of 20 and 60 years constitute the vast majority and represent 74.65% (n=53).

Figure 2 **GENDER DISTRIBUTION**

The female patients represent 50.7% (n=36) and the males represent 49.3% (n=35). The sex ratio male to female is 1:1.02.

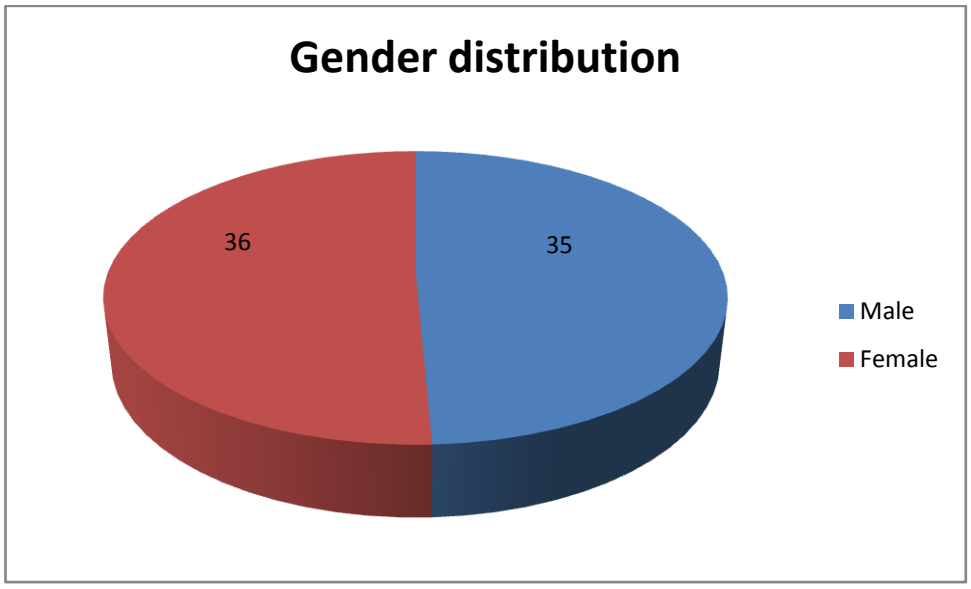


Figure 3 **PATIENTS DISTRIBUTION BETWEEN THE VARIOUS HOSPITALS**

The majority of the patients who had parotid surgery were found at Charlotte Maxeke Johannesburg Academic Hospital and represent 45.07% (n=32).

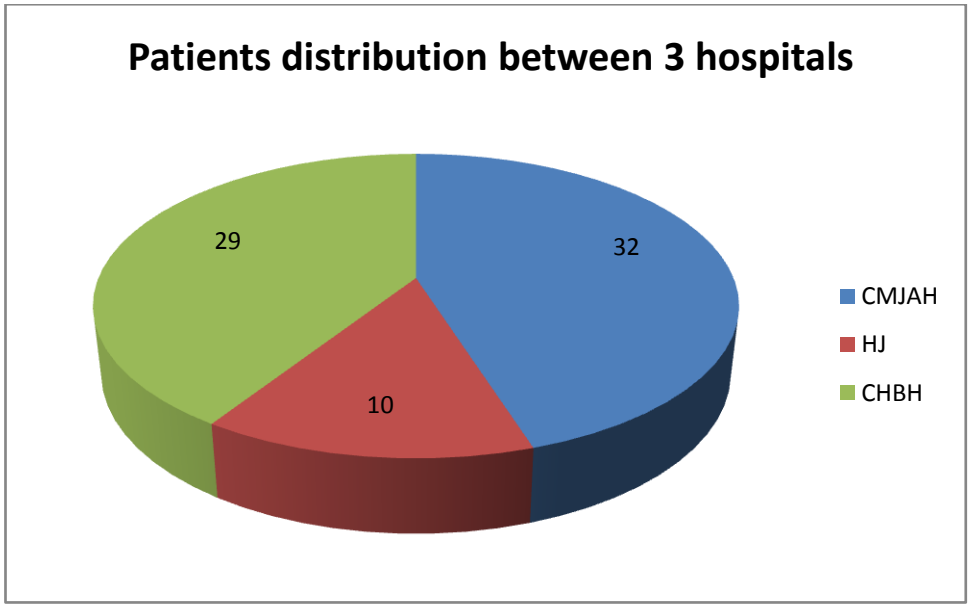


Figure 4: **Distribution of patients who had parotid surgery between year 2006 to 2010**

There is no significant difference in number of patients who had parotid surgery during different years included in our study. It ranges between 15.49% (n=11) and 23.94% (n=17).

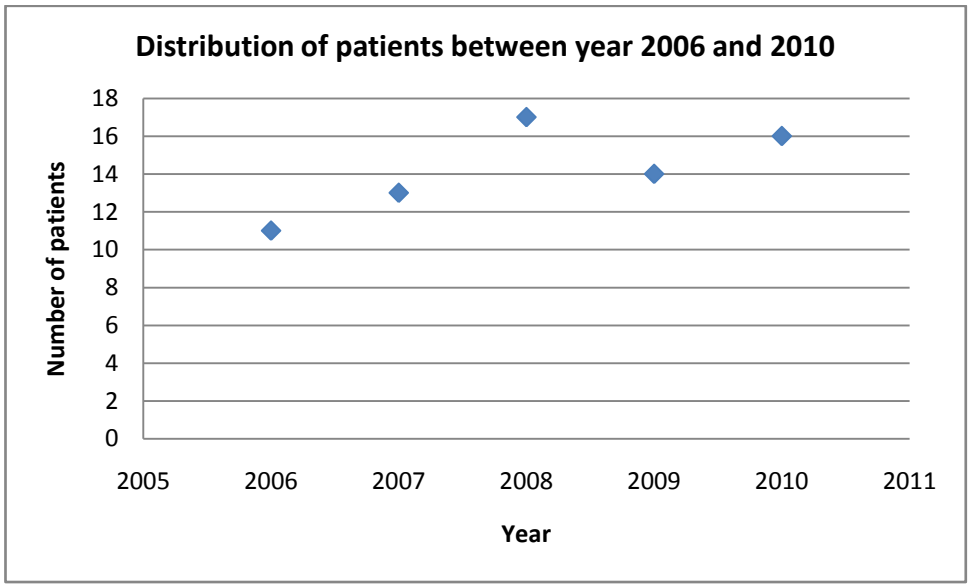


Table 1: DEMOGRAPHIC CHARACTERISTICS BY GENDER

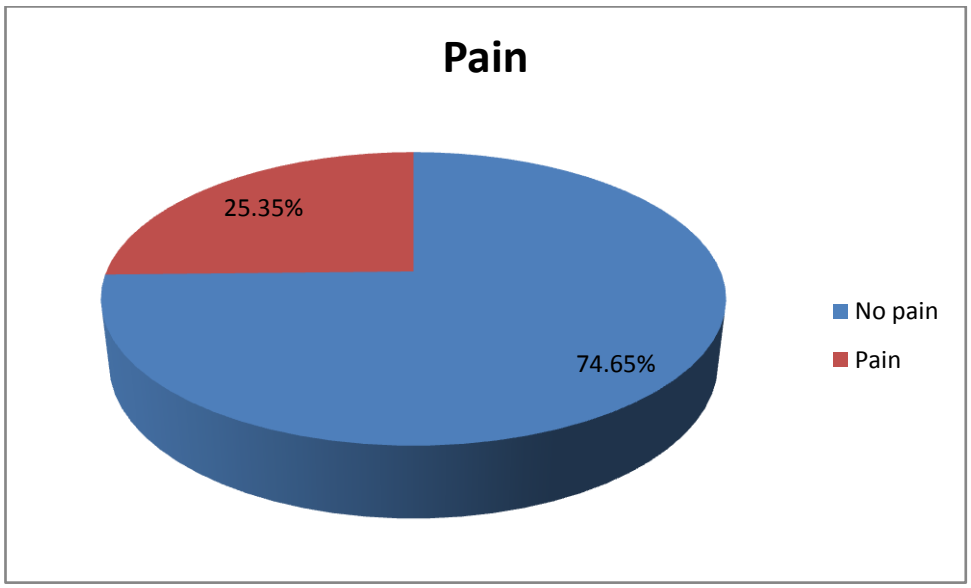
Variables	Males	Females
Age		
<20	1 (2.86%)	2 (5.56%)
20-40	11 (31.43%)	17 (47.22%)
41-60	14 (40%)	11 (30.56%)
>60	9 (25.71%)	6 (16.67%)
Hospital		
CMJAH	17 (48.57%)	15 (41.67%)
HJH	4 (11.43%)	6 (16.67)
CHBH	14 (40%)	15 (41.67%)
Year		
2006	7 (20%)	4 (11.11%)
2007	4 (11.43%)	9 (25%)
2008	10 (28.57%)	7 (19.44%)
2009	5 (14.29%)	9 (25%)
2010	9 (25.71%)	7 (19.4%)

In males, the majority of parotid tumours occurred in the age group between 41 and 60 years and represented 40% (n=14); and the age group between 20 to 40 years represented 47.22% (n=17) in females.

There was no gender difference between the different teaching hospitals.

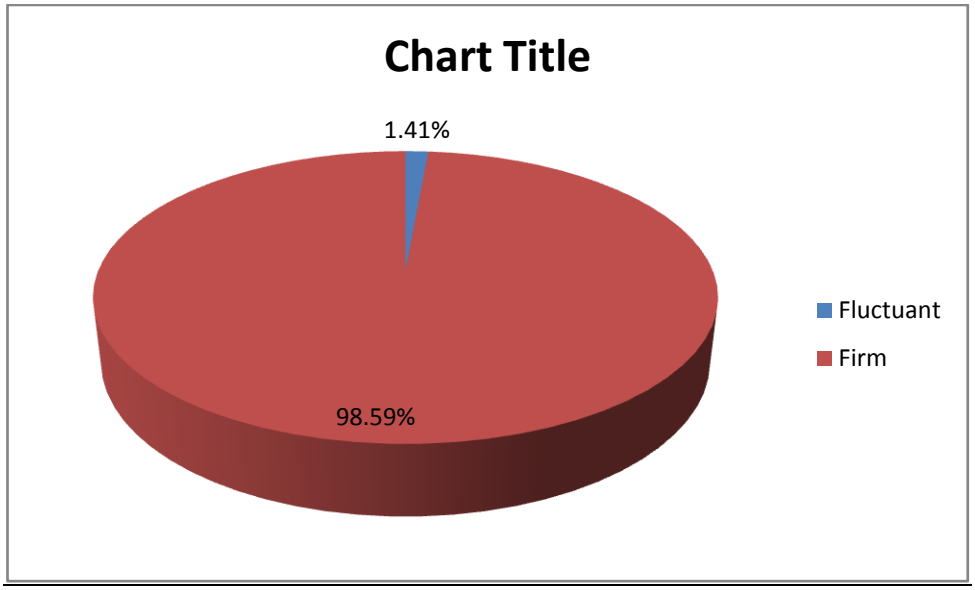
CLINICAL SIGNS

Figure 5: **PAIN.**



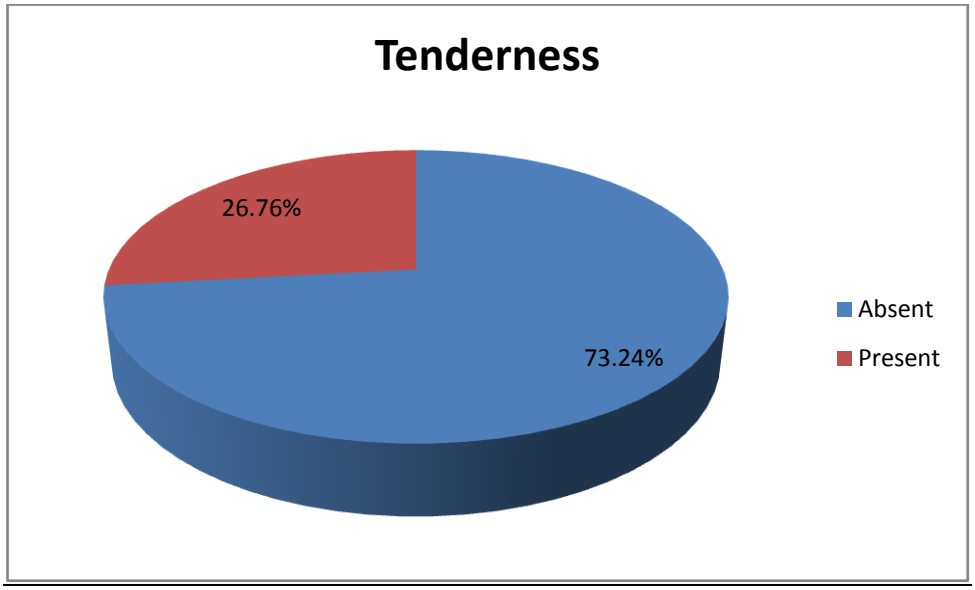
The majority of patients with parotid neoplasm's did not experience pain. The pain was present in 25.35% (n=18) of the patients.

Figure 6: **PHYSICAL CONSISTENCY**



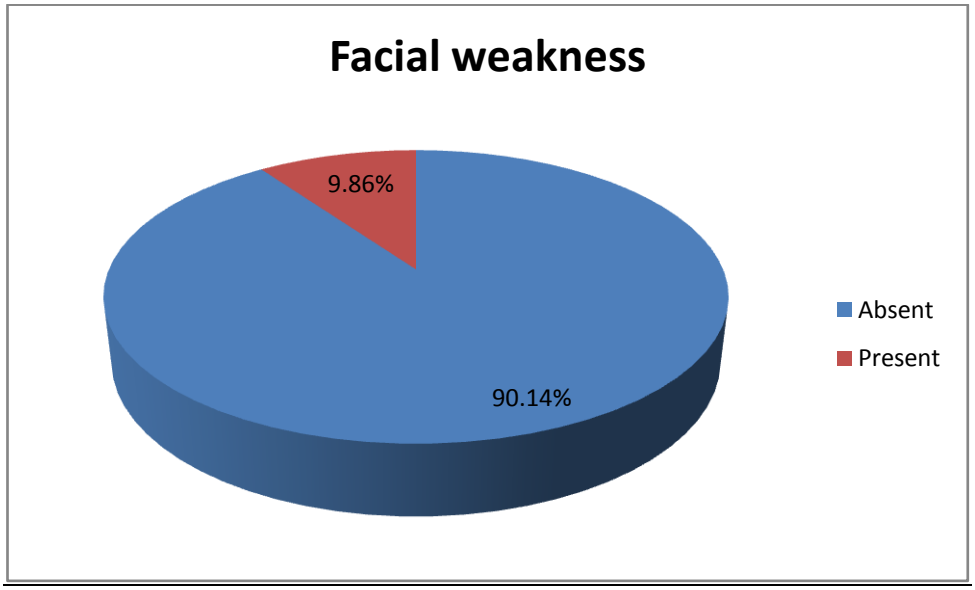
In our study, the majority of parotid neoplasm's were firm, only 1.41% (n=1) of patients had a fluctuant mass.

Figure7: **TENDERNESS**



The parotid tumours were tender in 19 patients representing 26.76% of the patients included in our study.

Figure 8: **FACIAL WEAKNESS**



The majority of the patient didn't have facial weakness; the facial nerve was involved in 7 patients representing 9.86%.

SWELLINGS IN PAROTID REGION

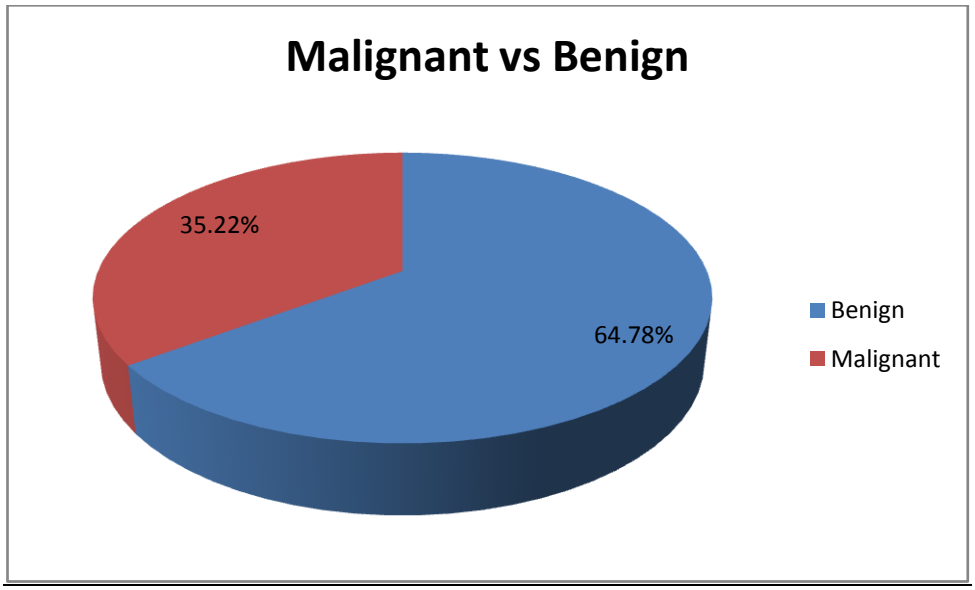
All patients presented with a palpable mass in the parotid region.

Table 2: **Table summarizing the clinical signs**

Clinical signs	n	%
Pain		
Absent	53	74.65
Present	18	25.35
Consistency		
Fluctuant	1	1.41
Firm	70	98.59
Tenderness		
Absent	52	73.24
Present	19	26.76
Facial weakness		
Absent	64	90.14
Present	7	9.86

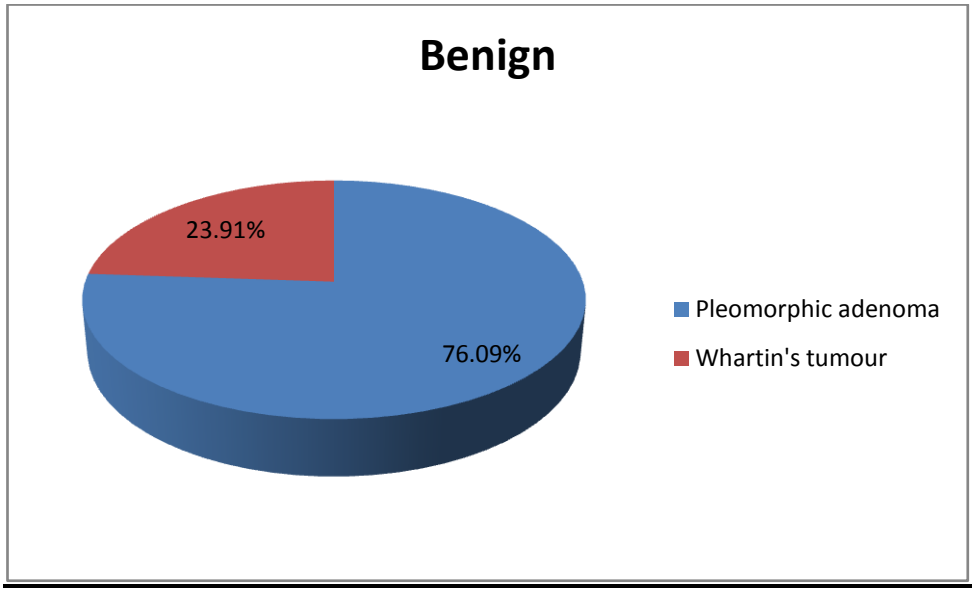
HISTOLOGICAL CHARACTERISTICS

Figure 9: **Distribution of Malignant versus Benign parotid tumours**



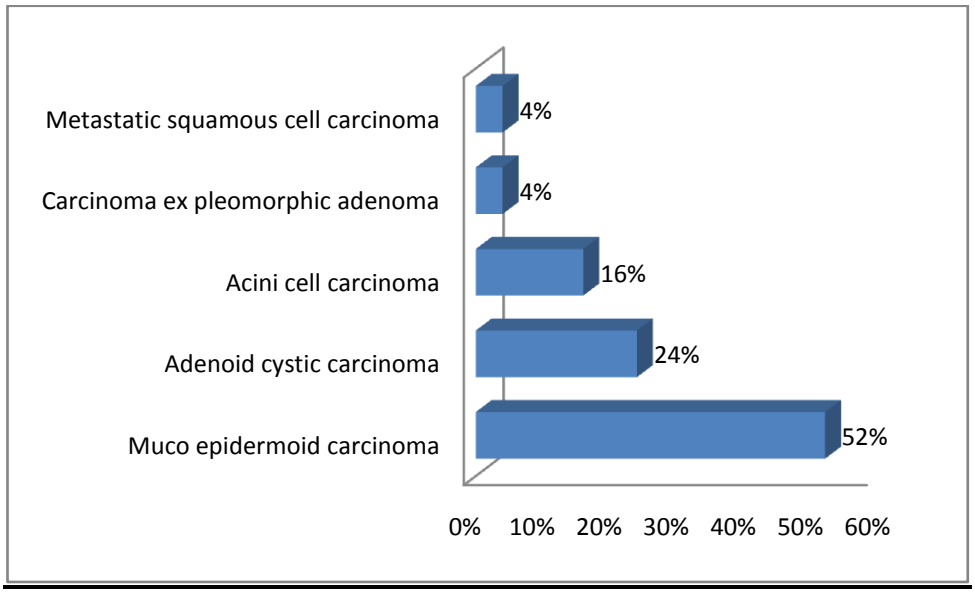
In our study, the majority of parotid tumours were benign and represented 64.78% (n=46); and malignant tumours represented 35.22% (n=25).

Figure 10: **Distribution of benign tumours**



Pleomorphic adenoma is the most common benign tumour and represent 76.09% (n=35); Whartin's tumours constitute 23.91% (n=11)

Figure 11: **Distribution of Malignant Tumours**



Muco-Epidermoid Carcinoma represents 52% (n=13) of malignant parotid tumours; adenoid cystic and acini cell carcinomas were present in 24% (n=6) and 16% (n=4) respectively.

Table 3: Histological characteristics by gender

Type of tumour	Male	Female
Benign		
Pleomorphic adenoma	**14(40%)**	**21(58.35%)**
Whartin's tumour	7(20%)	4(11.11%)
Malignant		
Mucoepidermoid ca	**7(20%)**	**6(16.67%)**
Adenoid cystic ca	3(8.57%)	3(8.33%)
Acini cell ca	2(5.71%)	2(5.56%)

In both males and females, pleomorphic adenoma and mucoepidermoid carcinoma were the most common benign and malignant tumours respectively.

Table 4: Difference between benign and malignant neoplasms with reference to clinical signs

Signs	Benign	Malignant	P value
No pain	40 (86.67%)	13 (52%)	**0.002**
Pain	6 (13.33%)	12 (48%)	
No facial weakness	45 (97.8%)	19 (76%)	**0.003**
Facial weakness	1 (2.2%)	6 (24%)	
No tenderness	39 (84.7%)	13 (52%)	0.007
Tenderness	7 (15.3%)	12 (48%)	
Firm	46 (100%)	24 (96%)	0.393
Fluctuant	0 (0%)	1 (4%)	

Analysis of the relationship between the clinical signs and the type of tumour (benign and malignant) was done using the Pearson Chi2 test. This showed a significant statistical difference for pain (p=0.002) and facial weakness (p=0.003). However, there was no statistical difference for tenderness (p=0.007) and consistency (p=0.393).

Table 5: Difference between benign and malignant neoplasm's with reference to gender and age.

	Benign	Malignant	p value
Male	20 (43.5%)	14 (56%)	0.46
Female	26 (56.5%)	11 (44%)	
<20	2 (4.3%)	1 (4%)	
21-40	17 (36.9%)	10 (40%)	0.388
41-60	18 (39.1%)	7 (28%)	
>60	8 (17.4%)	7 (28%)	

Analysis using the Pearson Chi2 showed no statistical difference between the type of tumour and gender (p=0.46) on one hand, and the age (p=0.388) on the other hand.

DISCUSSION

In this study, we analysed the clinical and histopathological findings from 71 patients diagnosed with parotid tumours at the University of Witwatersrand's Academic Hospitals, namely the Charlotte Maxeke Johannesburg Academic Hospital, Helen Joseph Hospital and Chris Hani Baragwanath Hospital over a period of 5 years, from 2006 to 2010.

All patients included in this study underwent parotid surgery for parotid neoplasms and the specimens were sent for histological analysis.

Most of the surgeries were performed at the Charlotte Maxeke Johannesburg Academic Hospital; representing 45.02%.

There was no significant difference in number of parotid surgery performed each year.

In this series, the mean age was 44 with a range of 7-81 years. The majority of the patients were between the age of 20 and 60 years. Our findings can be correlated to the Cape Town series which showed a mean age of 47.9 and a range of 6-93[(3).]

The mean age was high in Australian and Polish series compare to our findings, it was 54 with a range of 21-80 and 57.2 with a range of 4-84 respectively [(14, 4).]

There was no difference between males and females; the sex ratio male to female was 1:1.02. The Cape Town series showed a predominance of females for benign tumours and males for malignant tumours [(3).]

THE CLINICAL SIGNS

The majority of the patients did not experience pain. Pain was present in 18 patients representing 25.35%.

In our series, the initial presentation was a presence of a mass in the parotid region.

The parotid mass was firm in 70 patients (98.59%) and the mass was tender on palpation in 19 patients (26.79%).

In 2 studies done in Turkey and in the United States of America; the pattern of clinical signs in patients with parotid tumours [2,5] was very similar.

COMPARING THE HISTOPATHOLOGY

71 patients with parotid tumours were included in this study. Among them, 46 had benign and 25 malignant tumours representing 64.78% and 35.22% respectively. Our findings are comparable to those from Cape Town's series in which 31% were benign and 69% were malignant [3].

Studies from Nigeria and Tanzania reported malignancy in 44.3% and 46% of salivary gland tumours respectively [7, 8].

In most of western series, the rate of parotid malignancy is low compared to our findings. In studies from United States of America and Turkey, parotid malignancy represented 18% and 17% respectively [16, 2].

Australia constitutes an exception where 42% of parotid tumours are malignant [14].

- Pleomorphic adenoma was the most common benign parotid tumour representing 76.09%. Whartin's tumour accounted for 23.91%.

Pleomorphic Adenoma was found to be the commonest benign parotid tumour in all African and Western series.

- Whartin's tumour was found to be rare in other African series, they accounted for 2.5%, 0% and 9% in Nigeria, Tanzania and Cape Town (7,8,2).

Our results were comparable to the western series where they accounted for 21%, 28% and 14% in Canada, Australia and Italy respectively (5, 14, 17).

Muco-Epidermoid Carcinoma was the commonest malignant parotid tumour accounting for 52%. Adenoid cystic carcinoma, acini cell carcinoma, metastatic squamous cell carcinoma, and Carcinoma-ex-Pleomorphic carcinoma accounted for 24%, 16%, 4%, 4% respectively.

In series from Cape Town and Australia, metastatic squamous carcinoma was the commonest malignant tumour and accounted for 23% and 47% respectively (2, 14).

Muco-Epidermoid carcinoma was the commonest malignant tumour in series from United States of America, Pakistan and Nigeria and accounted for 31%, 60% and 15% respectively (16, 12, 7).

<u>Difference between Benign and Malignant Parotid Tumours with reference to Clinical Signs:</u>

In parotid tumours, symptoms such as pain and facial weakness are often regarded as clinical indicators of malignancy.

In our series, the pain was present in 6 patients (13.33%) with benign tumours and 12 patients (48%) with malignant tumours.

The facial nerve was involved In 6 patient (24%) with malignant tumours.

In the view of this data, it can be concluded that the clinical findings did carry a significant importance in the malignant-benign differentiation especially the presence of pain (p=0.002) and facial weakness (p=0.003).

Series from Turkey, Canada and Nigeria showed that pain and facial weakness were are regarded as indicators of malignancy [2, 5, 7].

Difference between benign and malignant parotid tumours with reference to gender and age.

In our series, there was no significant importance in the malignant-benign differentiation between males and females (p=0.46), and between different age groups (p=0.388).

In series from Cape town, benign tumours were common in females and malignant tumours in males[3].

CONCLUSION

The following conclusions are apparent from this study:

1. Benign parotid tumours are consistently more frequent than malignant tumours.

2. Pleomorphic adenoma is the most common of the benign parotid tumours.

3. Whartin's tumour has a high rate compared to other African series.

4. Mucoepidermoid carcinoma is the most common malignant tumour.

5. The malignant-benign ratio is comparable to other African series.

6. Pain and Facial Weakness are important clinical indicators of malignant disease.

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DATA COLLECTION SHEET

1. **AGE**
   - <20
   - 21-40
   - 41-60
   - >60

2. **GENDER**
   - Male
   - Female

3. **CLINICAL SIGNS AND SYMPTOMS**
   - Swelling
   - Pain
   - Facial Weakness
   - Skin Ulceration
   - Dysphagia
   - Fluctuation
   - Tenderness

4. HISTOLOGICAL TYPES

4.1 BENIGN

- Pleomorphic Adenoma
- Warthin's Tumour
- Myoepithelial Adenoma
- Basal Cell Adenoma
- Oncocytoma
- Others

4.2 MALIGNANT

- Muco-Epidermoid carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma
- Acini cell carcinoma
- Basal cell carcinoma
- Primary squamous cell carcinoma
- Metastatic squamous cell carcinoma
- Others