THE STUDY OF DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY OF SALIVARY GLANDS LESIONS IN HOSPITAL SULTANAH BAHIYAH

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (OTORHINOLARYNGOLOGY-HEAD AND NECK SURGERY)

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ABSTRAK (BAHASA MELAYU)

Pengenalan: Kadar penyakit pada kelenjar air liur merangkumi kira-kira 2 hingga 6.5 peratus daripada seluruh kes kanser kepala dan leher dalam kalangan orang dewasa. Pembengkakan di leher merupakan tanda-tanda awal yang biasanya dapat didiagnos melalui prosedur sitologi aspirasi jarum halus. Terdapat banyak kemungkinan sekiranya berlaku pembengkakan di kelenjar air liur seperti radang, jangkitan kuman atau kanser.

Objektif: Untuk menentukan ketepatan prosedur sitologi aspirasi jarum halus sebagai penilaian pra-pengendalian penyakit kelenjar liur di Hospital Sultanah Bahiyah (HSB) sebuah hospital rujukan bertaraf tertiari.

Kaedah: Semua pesakit yang telah menjalani pembedahan kelenjar liur dari Januari 2009 hingga Disember 2016 terlibat dalam kajian ini. Nilai ketepatan prosedur sitologi berbanding dengan histopatologi dikira antara penyakit ketumbuhan tidak bahaya dan kanser berdasarkan kepekaan sensitiviti, spesifik, nilai ramalan positif dan nilai ramalan negatif.

Keputusan: Seramai 138 pesakit telah menjalani pembedahan kelenjar air liur di HSB daripada tahun 2009 hingga 2016. Tujuh pesakit dikecualikan daripada kajian ini kerana tidak menepati kriteria. Daripada 131 pesakit, didapati nilai ketepatan diagnosis bagi kelenjar air liur adalah 72.5 peratus.

Kesimpulan: Prosedur sitologi aspirasi jarum halus adalah kaedah yang berguna dalam pemeriksaan penyakit kelenjar air liur yang boleh menjadi panduan kepada pakar bedah dalam rawatan lanjutan pesakit.

ABSTRACT (ENGLISH)

Introduction: Salivary glands lesions comprise about 2 to 6.5% of all head and neck neoplasms in adult. The common presentation is an enlarged mass which usually accessible for fine needle aspiration cytology. Enlargement or masses of the salivary gland have a wide differential diagnosis, as they can result from inflammatory responses, infectious lesions, or neoplasms.

Objective: To determine the accuracy of Fine Needle Aspiration Cytology (FNAC) as a pre-operative assessment of salivary glands lesions in Hospital Sultanah Bahiyah (HSB) a tertiary hospital.

Methods: All patients who had undergone salivary glands surgery from January 2009 to December 2016 were included. The diagnostic value of FNAC in comparison with histopathology was calculated for benign and malignant neoplasms based on sensitivity, specificity, positive predictive value and negative predictive value. The definitive histopathological diagnosis was compared with the preoperative FNAC diagnosis.

Results: There were a total number of 138 patients in HSB who had a pre-operative FNAC result and underwent salivary glands lesion surgery from 2009 to 2016. Total of 131 patients were included in this study. Seven patients were excluded in view FNAC was done at other centre. The overall FNAC accuracy in the diagnosis of salivary glands lesion was 72.5 per cent.

Conclusions: FNAC is a useful procedure as the diagnostic screening tool of salivary gland lesion as it can aid surgeon in patient's management.

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND OF STUDY

Salivary glands lesion comprises about 2 to 6.5% of all head and neck neoplasms in adult. The common presentation is an enlarged mass which usually accessible for fine needle aspiration cytology (FNAC). [1]

FNAC was first used for investigation of head and neck salivary gland lesion in the 1920s in Europe and United States. The procedure was thoroughly developed in the 1960s by the Karolinska Institute in Stockholm and the Institute Curie in Paris and popularised in the 1970s. [2]

At present, the accuracy of FNAC is improved by utilization of tumour marker studies, special stains and modern imaging techniques.[3] Enlargement or masses of the salivary gland have a wide differential diagnosis, as they can result from neoplastic or non-neoplastic lesion such as inflammatory responses and infectious disease. Most neoplasms are benign, but approximately 15% are malignant.[4]

FNAC had been used for many years as initial diagnostic tools. It is safe and causes minimal pain. It helps to differentiate between non-neoplastic, benign, and malignant lesions and subsequently influences decision for further management of the swelling which could either be surgical intervention or conservative management. The gold standard of the diagnosis is still by histopathological diagnosis. [4]

Despite being a technique used regularly in salivary gland tumours since the 1980s, its effectiveness in interpreting neoplastic lesions is still controversial.[5] This is mainly due to the great variety of morphological patterns, cell diversity and the overlapping of

histopathological findings among benign and malignant lesions of the salivary glands. This means that a small sample from the lesion, such as that obtained FNAC, at times does not provide an overall view of the morphological spectrum of the tumour.[5]

1.2 ANATOMY OF SALIVARY GLANDS

Salivary glands are compound, tubular, acinus, exocrine glands whose ducts open into the oral cavity. The salivary glands comprise the parotid, submandibular and sublingual glands, together with minor glands scattered over the labial, buccal, palatal and lingual surfaces of the oral cavity.

The parotid gland is the largest of the salivary glands producing mainly serous saliva (Figure 1). It covers the area anterior to the tragus of the external ear from the zygomatic arch superiorly to the upper neck inferiorly. It is shaped like a wedge, lying between the ramus of the mandible anteriorly and the temporal bone posteriorly. Its deep lobe occupies the pre-styloid component of the parapharyngeal space and approaches the lateral wall of the oropharynx. The parotid (Stensen) duct crosses the masseter, piercing the buccinator opening into the oral cavity opposite the second upper molar tooth. The facial nerve enters the parotid gland, dividing into two main divisions and five branches (temporal, zygomatic, buccal, mandibular and cervical), splitting the parotid gland into its superficial and deep lobes. The nerve is motor to the muscles of facial expression, sensory to a small patch of the external ear canal and special sensory to the anterior two-thirds of the tongue.[6]

The submandibular gland produces mixed mucinous and serous saliva, accounting for the majority of the saliva at rest (Figure 1). The gland lies between the mandible superiorly, the anterior belly of the digastric muscle antero-inferiorly and the posterior belly of digastric postero-inferiorly. The gland is divided into superficial and deep lobes as it hooks around the posterior border of the mylohyoid muscle. Superficially the gland is covered by the deep

layer of investing cervical fascia. The mandibular and cervical branches of the facial nerve lie on this. The deep lobe lies on the hyoglossus muscle medially, with the lingual nerve positioned superiorly and the hypoglossal nerve inferiorly. Wharton's duct runs anteriorly to open into the oral cavity lateral to the frenulum of the tongue.

The sublingual glands lie deep to the mucosa of the floor of the mouth between the mylohyoid and genioglossus muscles, opening directly onto the mucosa, or into the submandibular ductal system (Figure 1).

The minor salivary glands of the mouth include the buccal, labial, lingual, palatal and palatoglossal glands. The buccal and labial glands contain both mucous and serous elements. The palatal glands are mucous glands. They are located in both the soft and hard palate. The anterior and posterior lingual glands are mainly mucous. The anterior glands are embedded within muscle near the ventral surface of the tongue and open by means of four or five ducts near the lingual frenum. The posterior glands are located in the root of the tongue. Around the circumvallate papillae are serous glands (of Von Ebner). The palatoglossal glands are mucous glands and are located around the pharyngeal isthmus.

They secrete approximately 500 ml of saliva a day. Saliva lubricates the food with its mucous content, moistens the buccal mucosa, provides the aqueous medium which is essential for taste, secretes amylase and secretes the antimicrobials immunoglobulin A and lysozyme.[7]

Salivary flow rates are approximately 0.3 mL/min when unstimulated, rising to 1.5–2 mL/min when stimulated. During sleep, salivary flow rate is negligible. In the unstimulated state, the parotid gland contributes approximately 20 percent, the submandibular gland approximately 65 percent and the sublingual and minor salivary glands are the remainder.[8]

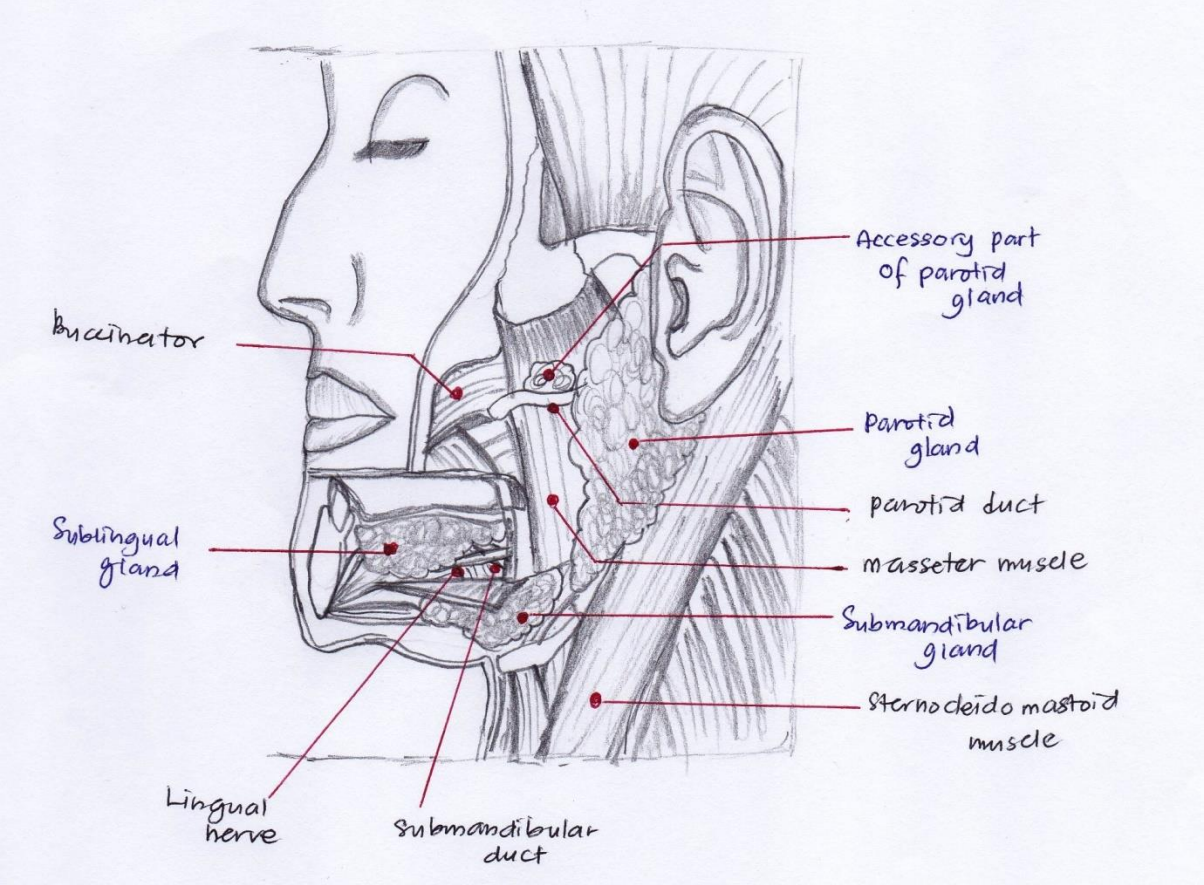

Figure 1: The parotid, submandibular and sublingual glands with their relations

1.3 MICROSCOPIC ANATOMY OF SALIVARY GLANDS

The basic secretory unit is the acinus, comprising secretory cells arranged in a sphere surrounding a duct. The secretory unit consists of acinus cells, myoepithelial cells, intercalated duct, striated duct and excretory duct.

1.4 SALIVARY GLANDS LESIONS

Salivary glands lesion can be divided into neoplastic disease, non-neoplastic disease, benign soft tissue lesions and haematolymphoid tumours. Neoplastic lesion can be further divided into malignant and benign tumour. Most (70%) salivary gland tumours are found in the parotid gland with 8% in the submandibular glands and 22% in the minor glands.[7]

1.4.1 BENIGN EPITHELIAL NEOPLASM

The World Health Organization (WHO) in 2017 classified benign tumours into 11 subtypes (Table 1). Because of the epithelial and myoepithelial tissue components of salivary glands, the tumours are a heterogeneous group which can be defined according to their dominant tissue type or can be mixed.

Pleomorphic adenoma (PA) is the most common tumour of the salivary glands. It is most frequently found in the parotid gland. This tumours are slow growing tumours and mainly present with painless mass. PAs are of mixed origin and the epithelial, myoepithelial and mesenchymal components demonstrate huge cell variation, architecture and morphology (Figure 2). Aspiration preparations contain variable combinations of bland ductal epithelial cells, myoepithelial cells, and chondromyxoid stroma. Surgical excision is the preferred management for these tumours as they have a small but definite potential for malignant transformation.

Warthin tumour also known as adenolymphoma, papillary cystadenoma lymphomatosum and cystadenolymphoma is the second most common benign neoplasm. Warthin tumour is cystic and found exclusively in the parotid glands. Ten percent are bilateral and there is an association with smoking and radiation exposure. Recent evidence questions whether Warthin tumours are truly parotid neoplasms, or rather are a disease of the periparotid lymph nodes. [8] Where possible, the management of these tumours is surgery.

The remaining benign epithelial neoplasms make up about 15% of all tumours. Their diagnosis depends on expert cytologist and histopathologist to determine benign from malignant processes. The final diagnosis of a salivary gland neoplasm can often only be made on definitive histology, one of the main reasons for performing surgery on clinically benign lesions.

Table 1: World Health Organization classification of epithelial salivary glands neoplasms

Benign epithelial neoplasms	**Malignant epithelial neoplasms**
Pleomorphic adenoma	Mucoepidermoid carcinoma
Myoepithelioma	Adenoid cystic carcinoma
Basal cell adenoma	Acinic cell carcinoma
Warthin tumour	Polymorphous adenocarcinoma
Oncocytoma	Clear cell carcinoma
Lymphadenoma	Basal cell adenocarcinoma
Cystadenoma	Intraductal carcinoma
Sialoadenoma papilliferum	Adenocarcinoma, not otherwise specified
Ductal papillomas	Salivary duct carcinoma
Sebaceous adenoma	Myoepithelial carcinoma
Canalicular adenoma and other ductal adenoma	Epithelial-emyoepithelial carcinoma
	Carcinoma ex-pleomorphic adenoma

Benign non epithelial neoplasms Haemangioma Lipoma/sialolipoma Nodular fasciitis **Non neoplastic lesions** Sclerosing polycystic adenosis Nodular oncocytic hyperplasia Lymphoepithelial sialadenitis Intercalated duct hyperplasia **Haematolymphoid tumours** Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)	Secretory carcinoma Sebaceous adenocarcinoma Carcinosarcoma Poorly differentiated carcinoma - Undifferentiated carcinoma - Small cell neuroendocrine carcinoma - Large cell neuroendocrine carcinoma Lymphoepithelial carcinoma Squamous cell carcinoma Oncocytic carcinoma Uncertain malignant potential Sialoblastoma

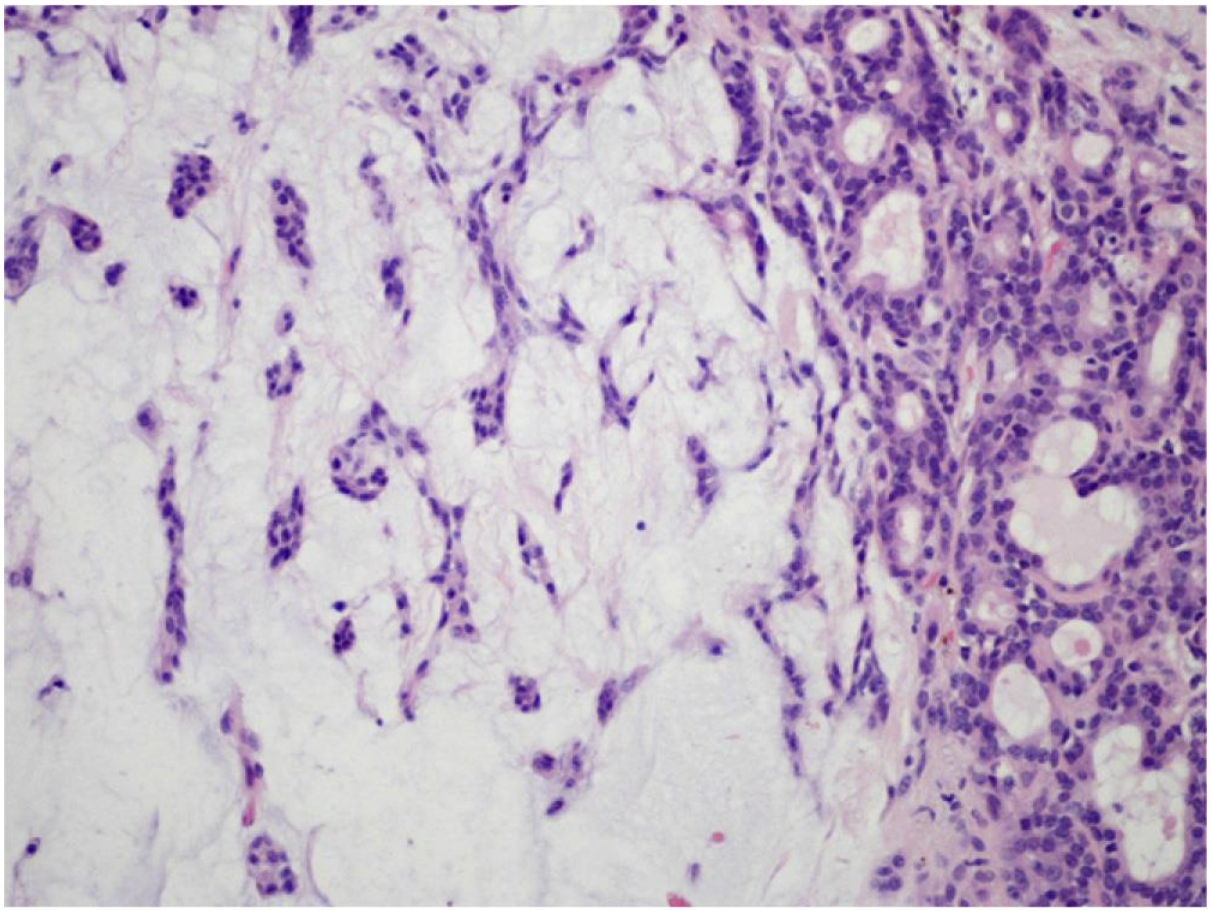

Figure 2: A pleomorphic adenoma composed of ductal structures that contain mucus secretions (right of field), along with dispersed reticular networks of cells embedded in a myxoid matrix (left of field). (Bradley P, O'Hara J, Wilson J. The salivary glands. Endocrine Surgery E-Book: Companion to Specialist Surgical Practice. 2013; 21: 191.)

1.4.2 BENIGN NON- EPITHELIAL NEOPLASMS

Haemangiomas commonly affect the parotid gland in children. The tumours have a characteristic rapid growth phase in the first 6 months. The diagnosis is entirely clinical and reassurance can be provided that natural resolution will occur between 1 and 2 years of age.

Another type of non-epithelial neoplasm is lipoma or sialolipoma. It is usually slow growing and clinically asymptomatic. Most of lipomas develop in the parotid glands. They develop rarely in the submandibular glands and very rarely in the minor salivary glands.

1.4.3 MALIGNANT EPITHELIAL NEOPLASMS

The most recent WHO classification of malignant salivary gland neoplasm includes 24 subtypes (Table 1) [7]. The majority, 60-70%, of patients will have either mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma or polymorphous low-grade adenocarcinoma.

Clinical signs that suggest a malignant tumour in the salivary gland include, pain, facial or hypoglossal nerve involvement, a sudden increase in size of a pre-existing salivary gland tumour and associated cervical lymphadenopathy.

Mucoepidermoid carcinoma is the most common malignant neoplasm of the salivary glands. Half of these tumours present in the major glands, frequently in the parotid gland (45%). The majority of tumours are low or high grade, are treated surgically and have a good prognosis but high-grade tumours have an increased metastatic potential.

Adenoid cystic carcinoma makes up 10% of malignant salivary gland tumours but 30% of minor salivary gland tumours. The tumours have a predilection for perineural spread and may present with nerve palsy. Despite local control with surgery and radiotherapy, 80 to 90% of patients die of the disease after 10 to 15 years due to metastases to the lungs, bone, brain and liver.

About 80% of acinic cell carcinoma occurs in the parotid gland. Presentation is a slow-growing mass, occasionally with pain and facial nerve palsy and may be bilateral. Acinic cell carcinomas tend to metastasize to the cervical lymph nodes.

Carcinoma ex-pleomorphic adenoma is those in which a new malignancy has arisen in a previous PA. They represent 12% of malignant salivary gland tumours and frequently present

as a long-standing mass that has recently increased in size. The treatment of choice is wide local surgical excision with neck dissection followed by postoperative radiotherapy.

Another type is metastatic disease to the major salivary glands. Parotid gland is the gland most frequently involved by metastatic disease usually by cutaneous squamous cell carcinoma of the head and neck. Whilst this is relatively rare in the northern hemisphere, it is the commonest parotid malignancy in Australia and New Zealand. The parotid gland has a lymphatic network which drains the temple and cheek regions; common sites for skin cancer. Metastases from infra clavicular primary sites are rare, with the literature limited to case reports from the lung, breast and kidney.

1.4.4 NON-NEOPLASTIC LESIONS

Non-neoplastic lesions of salivary glands range from inflammatory disorders of infectious, granulomatous or autoimmune aetiology to obstructive, developmental and idiopathic disorders.

These often present clinically as tumours and may have pathological features similar to some of the neoplasms yet making the diagnosis is difficult. Examples of non-neoplastic epithelial lesions from latest WHO Classification of Head and Neck Tumour 2017 are sclerosing polycystic adenosis, nodular oncocytic hyperplasia, lymphoepithelial sialadenitis and intercalated duct hyperplasia.

The other examples of non-neoplastic lesions of salivary glands are sialodenosis, tuberculosis, mucocele and sialadenitis. Sialoadenosis, or sialosis, is an uncommon, non-neoplastic, non-inflammatory enlargement of salivary gland acinar cells. In our study, we focus more on neoplastic lesions of salivary gland as well as some of non-neoplastic lesions which require surgical intervention.

1.5 FINE NEEDLE ASPIRATION CYTOLOGY

FNAC has been used for many years as an initial diagnostic tool. It is safe, cost-effective, and well tolerated by most patients, and it allows for quick, often unequivocal diagnosis. Salivary gland cytology helps differentiate non-neoplastic, benign, and malignant lesions.

Surgical management is often influenced by cytologic findings. Most of the benign salivary gland lesions are treated with superficial parotidectomy alone, whereas high-grade carcinomas are treated with total parotidectomy which some requiring facial nerve to be sacrifice. Lymph node neck dissection and neoadjuvant therapy are often indicated for high-grade tumours.

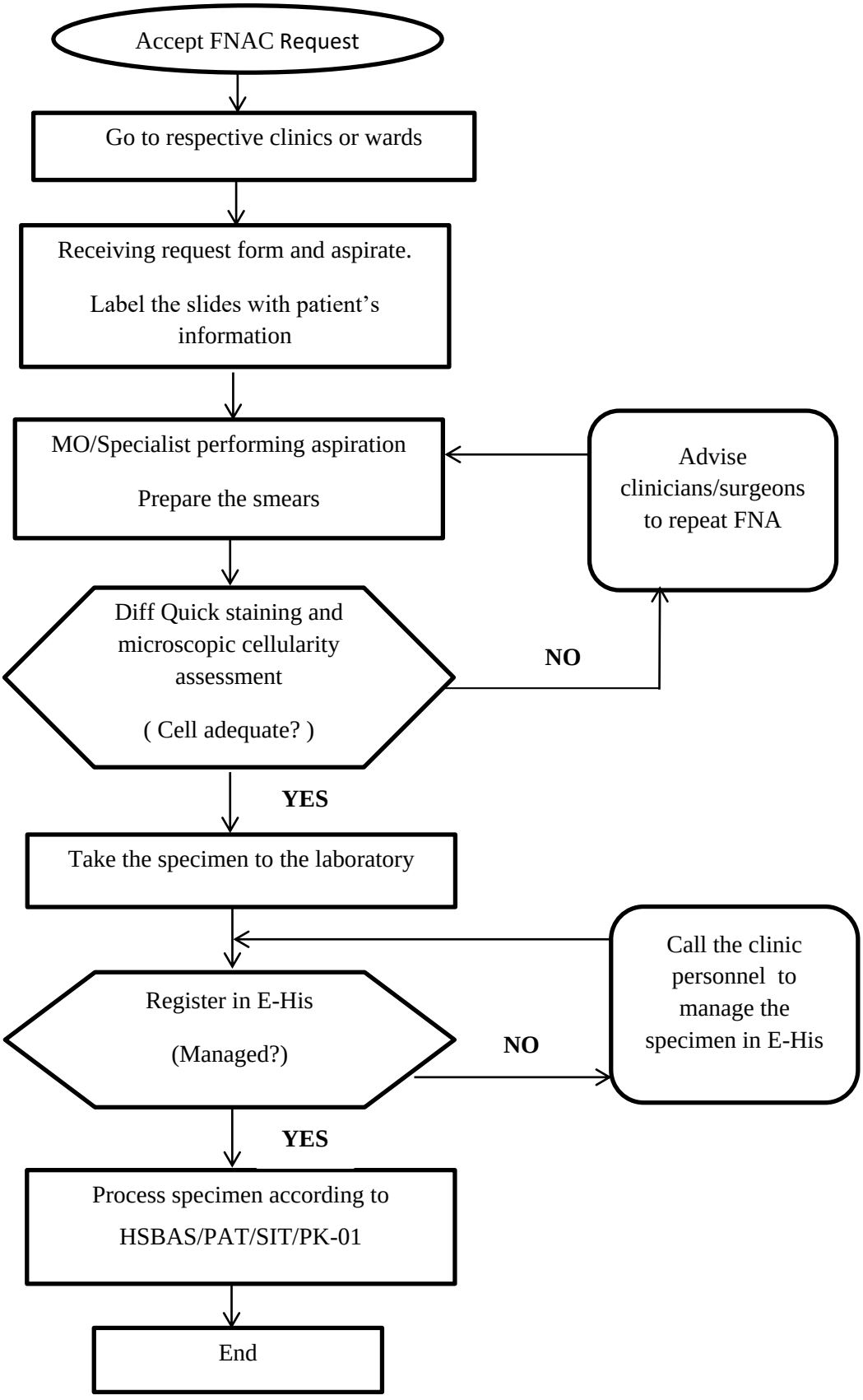

Figure 3: The Flow chart showed how the FNAC procedure handling in Hospital Sultanah Bahiyah

1.6 LITERATURE REVIEW

Previous studies have advocated the use of salivary glands cytology as an important diagnostic tool, with high sensitivity and specificity when used in conjunction with clinical evaluation and radiology.[9]

Others have reported mixed results, with sensitivities ranging from 55% to 98%, [2,5,9] and specificity ranging from 92% to 100%.[2,5,9]

Some studies report that it is less useful for malignant than benign lesions due to the varied histology and complexity of malignant salivary gland lesions that result in lower diagnostic accuracy. [9,10]

There are a few studies done in Malaysia before. Baharudin et al based on his study done in Universiti Sains Malaysia Hospital in 2010 found that the sensitivity of FNAC in detecting malignant disease was 57% with a specificity of 76% and positive predictive value of 36%. The overall FNAC accuracy in the diagnosis of parotid tumour was 74 per cent.[2] However this study only focused on parotid glands not other salivary glands. Most common false negative results are carcinoma of ex pleomorphic adenoma of parotid glands. In a study by Verma and Kapila all cases of carcinoma ex pleomorphic adenoma on histology were interpreted as benign on cytology and they concluded that it is difficult to identify carcinoma of ex pleomorphic adenoma on cytology. [11]

Another study done by Fereshteh et al in UKMMC found that FNAC had a sensitivity of 80% and a specificity of 98.8% for overall benign and malignant diagnoses and positive predictive and negative predictive values of 92.3% and 96.4% respectively.[1] This study also revealed that the most common false negative cases were pleomorphic adenoma(PA). FNAC is fairly accurate in diagnosing PA, occasionally problems may be encountered when differentiating PA from adenoid cystic carcinoma, monomorphic adenoma and mucoepidermoid carcinoma. All FNAC of unsatisfactory results were excluded from her study. [1]

Wu et al went on to assess the effectiveness of the use of ultrasonography (US) guidance for FNACs of the head and neck by a single cytopathologist.[12] They reported significantly better specificity (86%) and negative predictive value (100%) in US-guided FNACs than in palpation guided FNACs, with excellent sensitivity and positive predictable value preserved.[13] Based on these results, Wu advocates for cytopathologist-performed FNAC with US guidance as the best option if the cytopathologist has adequate training and resources to learn sonographic procedures.[13]In our centre, there are limited numbers of cytopathologist, so most of FNAC usually perform by non-pathologists. US-guided FNAC will only be performed by a radiologist for difficult deep-seated lesions.

1.7 RATIONALE OF THE STUDY

FNAC is a standard procedure performed as the initial diagnostic tool for any salivary gland swellings. The reason we want to do this study is to look for the accuracy of the FNAC as a diagnostic tool in this centre. There are no similar studies done in Ministry of Health (MOH) Hospital in Malaysia before.

We also want to identify the possible weakness so that improvement such as initiation of hands on training or to provide more numbers of pathologists in MOH Hospital or even obtains special sessions with radiologist to perform US-guided FNACs that has been proven to be more accurate. The accuracy of the diagnosis is important as it help in further management for the patient.

Adequate sampling by trained medical officer and pathologist, high quality smear preparation and established diagnostic criteria can help to diagnose majority of common benign and malignant parotid gland neoplasms with a high level of accuracy.

CHAPTER 2

OBJECTIVES

2.1 GENERAL OBJECTIVE

1. To determine the accuracy of FNAC as a pre-operative assessment of salivary glands lesions

2.2 SPECIFIC OBJECTIVES

1. To evaluate the correlation between cytological findings of aspiration and the histological results observed after surgery
2. To identify the sensitivity and specificity of salivary glands FNAC
3. To determine the accuracy of salivary glands FNAC by negative predictive value and positive predictive value

CHAPTER 3

MANUSCRIPT

3.1 TITLE PAGE

TITLE : DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY OF SALIVARY GLANDS LESIONS IN HOSPITAL SULTANAH BAHIYAH

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MAIN DOCUMENT

TITLE: DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY OF SALIVARY GLANDS LESIONS IN HOSPITAL SULTANAH BAHIYAH

3.2 ABSTRACT:

Background: Salivary glands lesions comprise about 2 to 6.5% of all head and neck neoplasms in adult. The common presentation is an enlarged mass which usually accessible for fine needle aspiration cytology (FNAC). Enlargement or masses of the salivary gland have a wide differential diagnosis, as they can result from inflammatory responses, infectious lesions, or neoplasms.

Objective: To determine the accuracy of FNAC as a pre-operative assessment of salivary glands lesions in Hospital Sultanah Bahiyah (HSB) a tertiary hospital.

Methods: All patients who had undergone salivary glands surgery from January 2009 to December 2016 were included. The diagnostic value of FNAC in comparison with histopathology was calculated for benign and malignant neoplasms based on sensitivity, specificity, positive predictive value and negative predictive value. The definitive histopathological diagnosis was compared with the preoperative FNAC diagnosis.

Results: Total of 131 patients were included in this study. 6 patients were excluded in view FNAC was done at other centre and 1 tuberculosis case. FNAC had a sensitivity of 35.4% and a specificity of 94.0% for overall benign and malignant diagnoses and positive predictive and negative predictive values of 77.3% and 71.6% respectively. The overall FNAC accuracy in the diagnosis of salivary glands lesion was 72.5%.

Conclusions: FNAC is a helpful method in the diagnostic screening of salivary glands lesions that can guide the surgeon in further management choice of the patient. There are significant different between FNAC done by pathologist and non-pathologist. This is better if

ministry of health can provide more numbers of pathologists so that improvement can be done.

Keywords: *salivary glands lesions; fine needle aspiration; diagnostic accuracy; sensitivity; specificity.*

3.3 INTRODUCTION

Salivary glands lesion comprises about 2 to 6.5% of all head and neck neoplasms in adult. The common presentation is an enlarged mass which usually accessible for fine needle aspiration cytology (FNAC). [1]

FNAC was first used for investigation of head and neck salivary gland lesion in the 1920s in Europe and United States. The procedure was thoroughly developed in the 1960s by the Karolinska Institute in Stockholm and the Institute Curie in Paris and popularised in the 1970s. [2]

At present, the accuracy of FNAC is improved by utilization of tumour marker studies, special stains and modern imaging techniques.[3] Enlargement or masses of the salivary gland have a wide differential diagnosis, as they can result from inflammatory responses, infectious lesions, or neoplasms. Most neoplasms are benign, but approximately 15% are malignant.[4]

FNAC had been used for many years as initial diagnostic tools. It is safe and causes minimal pain. It helps to differentiate between non-neoplastic, benign, and malignant lesions subsequently influences decision of further management of the swelling either surgical intervention or conservative management. The gold standard is still by histopathological diagnosis. [4]

Despite being a technique used regularly in salivary gland tumours since the 1980s, its effectiveness in interpreting neoplastic lesions is still controversial.[5] This is mainly due to the great variety of morphological patterns, cell diversity and the overlapping of

histopathological findings among benign and malignant lesions of the salivary glands. This means that a small sample from the lesion, such as that obtained FNAC, at times does not provide an overall view of the morphological spectrum of the tumour.[5] The objective of this study is to determine the accuracy of FNAC of salivary glands lesions in our centre.

3.4 METHODOLOGY

3.4.1 STUDY DESIGN

This is observational, retrospective cross sectional study. This study was conducted in Hospital Sultanah Bahiyah Alor Setar, a tertiary hospital. All patients with history of salivary gland disease treated surgically for past 8 years experiences from 2009 to 2016 were traced.

The study was carried out after obtaining approval from Medical Research & Ethics Committee from HSB and Human Research Ethics Committee USM (HREC) from Hospital USM and conducted according to the Declaration of Helsinki. Retrieval of data at medical record unit was conducted.

3.4.2 INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria are all patients with salivary gland swellings with preoperative FNAC. Patient underwent FNAC but no surgical intervention done example parotid lymphoma or parotid tuberculosis was excluded from this study. We also excluded all patients who underwent FNAC but refuse surgery because of no gold standard histopathological result for comparison and case referred from outsource.

3.4.3 TOOLS

In the ENT department of HSB FNACs are performed using a 22-gauge needle attached to a 20 ml syringe holder by free hand technique. The specimens are expelled onto three or four slides, and thin smears are prepared between slides and immediately fixed. The slides are generally stained with Papanicolaou and occasionally with May-Grunwald Giemsa methods. Cytological diagnoses based on the fine needle aspiration smears are categorized into three

categories namely benign, malignant and suspicious. The gold standard for diagnosis is based on the histopathological findings from the subsequent biopsy. The results will then be compared with the findings of other previous studies.

3.4.4 STATISTICAL ANALYSIS

All the data are coded and entered into SPSS. A significant level of $p<0.05$ will be considered statistically significant.

The diagnostic value of FNAC in comparison with histopathology will be calculated for benign and malignant neoplasms using the following formula:

1) Accuracy = (True Positive + True Negative) × 100/(True Positive + True Negative + False Positive + False Negative).

2) Sensitivity = (True Positive × 100) / (True Positive + False Negative).

3) Specificity = (True Negative × 100) / (True Negative + False Positive).

4) Positive predictive value = (True Positive × 100) /(True Positive + False Positive).

5) Negative predictive value = (True Negative × 100) /(True Negative + False Negative).

3.5 RESULT

3.5.1 Demographics

There were a total number of 131 patients at our hospital who had a pre-operative FNAC result and underwent salivary gland surgery from 2009 to 2016. The demographic data and clinical characteristics of study subjects are as listed. (Table 1). Mean (SD) age of study subjects was 51.31 years. There were 64 males (48.9%) and 67 female (51.1%). Majority of the patients were Malay, which were about 98 (74.8%) followed by Chinese 25 (19.1%), Indian 5 (3.8%) and Siamese 3 (2.3%). The most common gland involved was parotid glands 109 (83.2%), followed by submandibular glands 19 (14.5%), minor salivary glands 2(1.5%) and sublingual gland 1(0.8%).

Table 1: Demographics and characteristic of the study subjects

Age	Mean	51.31	Percentage (%)
Races	Malay	98	74.8
	Chinese	25	19.1
	Indian	5	3.8
	Siamese	3	2.3
Gender	Male	64	48.9
	Female	67	51.1
Gland involvement	Parotid	109	83,2
	Submandibular	19	14.5

	Sublingual	1	0.8
	Minor salivary gland	2	1.5
Total		131	100%

3.5.2 Histopathological correlation

Histopathological correlation was available for all 131 cases. The lesions were histopathologically diagnosed as benign in 85 cases (65%), malignant in 30 cases (33%) and non-neoplastic in 16 cases (12%). (Table 2). The benign lesions included mostly pleomorphic adenomas PAs (44 cases), Warthin's tumours (25 cases), lymphadenoma (8 cases), basal cell adenoma (4 cases) and cystadenoma (4 cases).

On the other hand, majority of the malignant lesions is mucoepidermoid carcinoma (11 cases) followed by basal cell adenocarcinoma (5 cases) then oncocytic carcinoma, carcinoma of ex pleomorphic adenoma, squamous cell carcinoma, adenoid cystic carcinoma (3 cases) and metastatic sebaceous carcinoma 2 cases (Table 3).

Thirteen cases noted to be non-neoplastic lesions on histology. Majority is cyst (6 cases) followed by sialodenosis (4 cases), ranula (3 cases), Kimura disease (2 cases) and necrotising sialometaplasia (1 case).

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3.5.2.1 Benign lesions

Out of 44 PAs reported on FNA, 39 cases were confirmed as PA on histology. There were 5 discrepancies in the diagnoses. 4 cases turned out to be malignant 2 carcinoma of ex-pleomorphic adenoma, 1 basal cell carcinoma and 1 adenoid cystic carcinoma. Another 1

case is non-neoplastic lesion. Second most common benign lesion is Warthin tumour about 25 cases. Out of 25 cases, only 14 cases were diagnosed on FNAC. On the other hand, 5 cases of Warthin tumour turn to be non-neoplastic, 3 malignant lesions, 2 unsatisfactory and 1 pleomorphic adenoma on FNAC.

Table 2: Cross tabulation between Histopathological Diagnosis and Fine Needle Aspiration Cytology (FNAC) Diagnosis

FNAC diagnosis	Histopathological diagnosis			
	Benign	Malignant	Non-neoplastic	Total
Unsatisfactory	10(FN)	6(FN)	8(FN)	24
Benign	71(TN)	7(FN)	7(TN)	85
Malignant	4(FP)	17(TP)	1(FP)	22
Total	85(65%)	30(33%)	16(12%)	131(100%)

There was an association between cytological findings of aspiration and the histopathological results (p-value<0.001, Pearson chi-square=54.09).

Table 3: Histopathological Diagnosis

Benign lesion	**n=85**
Pleomorphic adenoma	44
Warthin tumour	25
Lymphadenoma	8
Basal cell adenoma	4
Cystadenoma	4