The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy

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SUBMITTED TO THE TRIBHUVAN UNIVERSITY
IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE
DEGREE OF DOCTOR OF MEDICINE
IN PATHOLOGY

BY
Dr. Shimal Thasneem

Kathmandu, Nepal, 2007

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A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Medicine in Pathology of the Tribhuvan University, Nepal

Dr. Shimal Thasneem

Based on the studies conducted at the Department of Pathology,
Tribhuvan University Teaching Hospital,
Kathmandu, Nepal.

Guide: Prof Gita Sayami
Department of Pathology,
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CERTIFICATE

This is to certify that the work contained in the thesis entitled **The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy** is the result of the original investigative study undertaken by Dr Shimal Thasneem in the Department of Pathology under our direct supervision and guidance.

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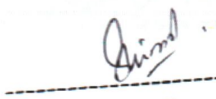
DECLARATION

I hereby declare that this thesis work on "**The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy**" has not been submitted in candidature for any degree. I will have no objection for availability of this thesis (as part or whole) for photocopied or used for other research purposes.



Dr Shimal Thasneem
September 2007

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Dedicated to my family

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LIST OF ABBREVIATIONS

TB LN	-	Tuberculous lymphadenitis
Reac LN	-	Reactive lymphadenitis
SCC	-	Squamous cell carcinoma
SmCC	-	Small cell carcinoma
PDC	-	Poorly differentiated carcinoma
Adenoca	-	Adenocarcinoma
NHL	-	Non-Hodgkin's lymphoma
HL	-	Hodgkin's lymphoma
Undiff ca	-	Undifferentiated carcinoma
FNAC	-	Fine needle aspiration cytology
HPE	-	Histopathological examination
TUTH	-	Tribhuvan University Teaching Hospital

Abstract

Introduction:

Lymphadenopathy is one of the commonest clinical presentations of patients attending the out patient department. The role of fine needle aspiration cytology in diagnosing lymphadenopathy has become widely accepted as a reliable, cost effective procedure that has several advantages over excisional biopsy.

Objectives:

The main objective of this study was to analyze the causes of cervical lymphadenopathy and to determine the role of fine needle aspiration cytology in diagnosing cervical lymphadenopathy.

Results:

A total of 299 cases of cervical lymphadenopathy presented for FNAC from November 2005- November 2006 to Department of Pathology, TUTH. Of which subsequent biopsy were available in 101 cases. The histopathological diagnosis of these 101 cases were compared with the FNAC diagnosis, taking biopsy as the gold standard.

Benign lesions constituted majority of conditions to present with enlarged cervical lymph nodes, comprising of 83%, and malignant metastasis constituting 17%. Of the benign lesions reactive lymphadenitis was the most prevalent (44%), followed by tuberculous lymphadenitis (37%). Squamous cell carcinoma (6%) was found to be the most common metastasis to cervical lymph node, mostly to upper

anterior group of cervical lymph nodes (5%). Posterior cervical lymph nodes were the most frequent lymph node groups to be involved (71%), followed by anterior cervical group (28%).

Senstivity and specificity of FNAC were found to be 98% and 100% respectively. For benign lesions, sensitivity and specificity were 98.8% and 100%, and for malignant lesions it was found to be 94.4% and 100%. The positive predictive value was 100% and negative predictive value was 99.7%. These findings were in accordance with several studies done previously.

Conclusion:

Therefore FNAC was found to be a useful, reliable method with high accuracy rate in determining the causes of cervical lymphadenopathy.

INTRODUCTION

FNAC has become an integral part of the initial diagnosis and management of patients presenting with lymphadenopathy. This simple technique has recently gained wide acceptance, since it offers a high degree of accuracy, lending itself to outpatient diagnosis and thus making savings in the cost of hospitalization. It has several advantages over excisional biopsy. The procedure requires minimal time, whereas on the other hand excisional biopsy often requires time away from work, preoperative investigations, exposure to risk of anesthesia and postoperative infections. [1]

FNAC is an easy and cost effective procedure which is patient friendly and a quick result can be obtained thereby enabling the surgeon to start treatment early, whereas biopsy is time taking, more painful causing unwarranted bleeding at times and delays the treatment because it needs more time for processing and hence reporting. In the developing third world countries where a blade carries a surgical impression and a needle enjoys a therapeutic image, the potential role of FNAC is far reaching.

Lympahadenopathy is one of the commonest clinical presentations of patients attending the outpatient department. Lymphadenopathy refers to nodes that are abnormal in either size, consistency or number. There are various classifications of lymphadenopathy , but a simple system is to classify lymphadenopathy as " generalized ", if lymph nodes are enlarged in two or more

non-contiguous areas or "localized" if only one area is involved. Approximately about three fourths of patients present with localized lymphadenopathy and about one fourth of patients present with generalized lymphadenopathy in a primary care setting. [2, 3 4] Cervical lymphadenopathy can result from a vast array of disease processes, representing infections, malignancies, autoimmune diseases, iatrogenic causes etc.

As cervical lymphadenopathy can present in diseases of variety of causes, the use of fine needle aspiration cytology in diagnosis of the causes of cervical lymphadenopathy has become an easy and effective method. More to it, the prognosis of a particular disease takes its toll by the use of this effective method.

In this study the diagnostic role of fine needle aspiration cytology and excision biopsy was compared, and the frequency of diseases causing cervical lymphadenopathy was evaluated.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

GENERAL-To analyse the causes of cervical lymphadenopathy.

SPECIFIC:

1. To determine the frequency of neoplastic and non-neoplastic diseases causing cervical lymphadenopathy.

2. To find out age and sex distribution of patients with cervical lymphadenopathy

3. To determine the sensitivity and specificity of FNAC in diagnosing the diseases causing cervical lymphadenopathy.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design- prospective

Study period- 1 year

Place- Department of Pathology , TUTH, Katmandu, Nepal

Sampling size- 100 cases of fine needle aspirated cases and subsequent excisional biopsy of the same lymph node.

INCLUSION CRITERIA

All excised lymph node biopsy specimens with fine needle aspirated lymph nodes, irrespective of age and sex, were included in this study.

EXCLUSION CRITERIA

Patients without consent.

Inadequate aspirates that were not available for repeat aspirations were excluded from the study.

PROCEDURE

The skin above the area to be aspirated was cleared with an antiseptic solution. After locating the mass a fine needle of 23 guage was passed through the mass. The needle was inserted and withdrawn several times, and the material aspirated by pulling the plunger of the syringe. After the needle was withdrawn the aspirate was blown onto the slide, and smears made. Two slides were immediately kept in propanolol for Papanicolaou stain and two slides were air dried for Giemsa stain. [5]

Papanicolaou method of staining

Smears were put in 95% alcohol

After fixation, slides were transferred without drying directly from alcohol to 90% alcohol, 80% alcohol , 70% alcohol and water to distilled water.

Stained in Harris haematoxylin (modified) for 10 minutes.

Rinsed in water to prevent cells from being washed off.

Differentiate carefully the nuclear staining in 1% hydrochloric acid and in 70% alcohol.

Placed gently in water for five minutes to wash out acid thoroughly and blue the nuclei.

Rinsed in distilled water and transfer through 70% alcohol.

Stained in OG 6 for 6-10 minutes.

Washed with 70% alcohol

Stained with EA 36 for 5 minutes.

Washed in 90%, 100% alcohols.

Put in xylene I and II

Mounted in DPX.

Giemsa Staining

Air dried smears were fixed in a jar of methanol for 20-30 minutes.

Stained with Giemsa stain diluted with nine parts of phosphate buffer for 20-30 minutes.

Washed with distilled water

Dried in air

Mounted with DPX.[6]

Specimen collection for histopathology

The patients were then subjected to lymph node excision biopsies. Patients underwent surgery at a later date and the surgical specimen subjected to histopathological examination.

The specimens were processed by the usual graded alcohol dehydration in the automated histokinette. An overnight schedule of 16-18 hours were used. The tissues were the embedded in paraffin wax and sliding microtome sectioning was done with a thickness of 3-4 microns. These sections were fixed in glass slides, dewaxed and made ready for staining with haematoxylin and eosin stains.

Haematoxylin and eosin staining

Dewaxed in xylene

Treatment through graded alcohol of decreasing concentration i.e. 100%, 90%, 80%, 70% to water.

Stained with Harris haematoxylin for 15 minutes.

Washed in water for five minutes.

Treatment in 1% acid alcohol (1% HCL in 70% alcohol) for 5-10 seconds.

Washed in water for 5 minutes, treatment with lithium carbonate for 1 minute.

Washed in water.

Stained with 0.5% eosin for 10 minutes.

Treatment through graded alcohol of increasing concentration i.e. 70%, 80%, 90%.

Treatment with xylene for clearance.

Mounted with DPX. [6]

LITERATURE REVIEW

Literature review

Anatomical considerations

The neck lymph nodes are divided into five major groups.

Significant Nodal Groups in the neck

Deep lateral cervical.

Submental-submandibular.

Parotid.

Retropharyngeal.

Anterior cervical.

Deep Lateral Cervical Group

A. Internal jugular chain (deep cervical).

B. Spinal accessory chain (posterior triangle).

C. Transverse cervical (supraclavicular).

The highest jugular digastric node near the angle of the mandible is called the "sentinel" node.

The "signal" node is the lowest along the internal jugular chain called the virchow nodes.

If only a virchow node is present, then one should check the abdomen and/or chest for primary source of metastasis.

The internal jugular chain is divided into:

High: Above the hyoid.

Mid: Between hyoid and cricoid.

Low: Below the cricoid.

The internal jugular chain is a common final pathway that receives drainages from parotid, retropharyngeal, and submandibular/submental groups. Drainage from the internal jugular chain is into the subclavian vein and/or internal jugular vein and/or into the right lymphatic duct and thoracic duct.

Spinal accessory (posterior triangle) nodal group receives occipital/mastoid, lateral neck, scalp, nasopharyngeal sources. Abnormal spinal accessory nodes may indicate the presence of an early nasopharyngeal cancer.

Transverse cervical chain receives drainage from deep cervical, supraclavicular, subclavicular, upper chest, anterior lateral neck.

Sources: The drainage is the same as for the internal jugular chain.

Submental/Submandibular Chain

Submental nodes receive drainage from adjacent skin, lips, floor of the mouth, and drain to the submandibular nodal group. Submandibular nodes are extra glandular and receive drainage from anterior face, floor of the mouth, anterior oral cavity, and submental nodal group. Drainage is to the high internal jugular chain.

Parotid Nodal Group

Intra or extra glandular nodes.

Receives drainage from external auditory canal, eustachian tube, adjacent skin, buccal mucosa (squamous cell carcinoma and melanoma of skin frequently metastasize to this group). Drainage is to high internal jugular chain.

Retropharyngeal Nodal Group

Two compartments: Medial and lateral retropharyngeal.

Medial retropharyngeal receives drainage from nasopharynx and oropharynx and drains to high internal jugular chain.

Lateral retropharyngeal (nodes of Rouvierre) are located just medial to the internal carotid artery. Drainage is the same as for the medial retropharyngeal nodes.

Early sign of nasopharyngeal cancer may be the presence of abnormal lateral retropharyngeal node in the patient over forty years.

Anterior Cervical Nodal Group

Anterior jugular: superficial. Follows the course of the external jugular vein. Receives drainage from skin and muscles of the anterior neck. Drains to the thoracic duct.

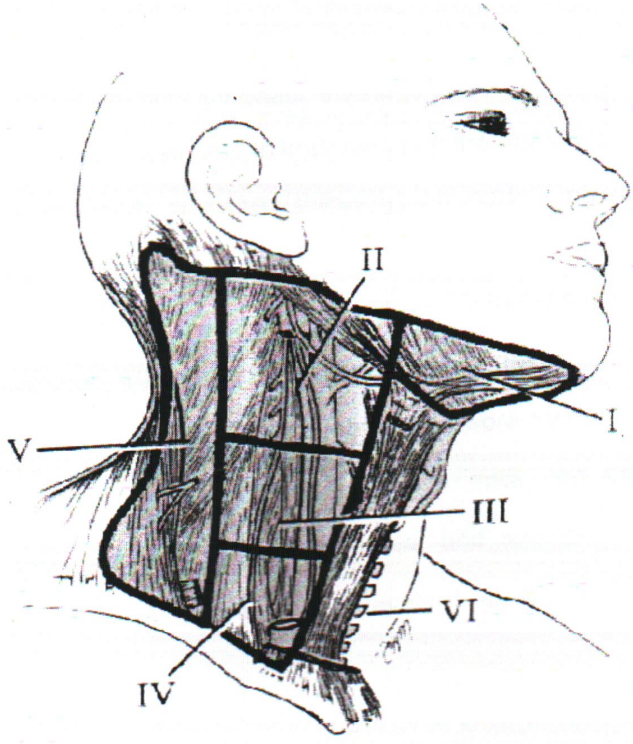
Paraesophageal group: Tracheal esophageal groove nodes and delphian node. Abnormal delphian node is often an indicator of subglottic laryngeal cancer

extension.

This group receives drainages from hypopharynx, larynx, thyroid, and esophagus. Drainage is then to the thoracic duct. [7]

Classification to describe the patterns of metastasis

The lymph nodes of the neck can be divided into six levels within the defined anatomic triangles. These groups and the areas that they drain are particularly important when locating and working up a "neck mass" or possible malignancy. The groups and drainage areas are as follows:



- **I--Submental and submandibular nodes**
- **II--Upper jugulodigastric group**

- **III--Middle jugular nodes** draining the naso- and oropharynx, oral cavity, hypopharynx, larynx.
- **IV--Inferior jugular nodes** draining the hypopharynx, subglottic larynx, thyroid, and esophagus.
- **V-- Posterior triangle group**
- **VI--Anterior compartment group** [8]

In his 1964 study of lymphatic drainage of this area, Fisch, using the technique of lymphography, was able to improve upon the anatomic classification proposed by Rouviere. Fisch classified these lymph nodes into 5 categories: junctional, jugular, spinal, supraclavicular, and retroauricular. However, the nomenclature in popular use today comes from the Memorial Sloan Kettering Cancer Center. This classification was used to describe the patterns of metastatic dissemination observed in more than 1000 patients who were treated at the center with radical neck dissection. Lymph nodes in the neck are grouped into levels I-V, corresponding with the submandibular and submental nodes (level I); upper, middle, and lower jugular nodes (levels II, III, IV); and posterior triangle nodes (level V).

Submental/ submandibular nodes (Level I)

These are bound by the body of the mandible superiorly, stylohyoid muscle posteriorly, and the anterior belly of the digastric muscle on the contralateral side

anteriorly. This level may be divided into level Ia, which refers to the nodes in the submental triangle (bound by the anterior bellies of the digastric muscles and the hyoid bone), and Ib, which refers to the submandibular triangle nodes. The nodes of level Ia are at greatest risk of harboring metastasis from cancers that arise from the floor of mouth, anterior tongue, anterior mandibular alveolar ridge, and lower lip, while the nodes of level Ib often receive metastasis from cancers of the oral cavity, anterior nasal cavity, soft tissue structures of the mid face, and submandibular gland.

Closely related, although not strictly a part of the level I group of nodes, are the perifacial nodes, related to the facial vessels above the mandibular margin, and the buccinator nodes, which may become involved with metastasis from tumors in the buccal mucosa, nose, and soft tissues of the cheek and lips.

Upper jugulodigastric group (Level II)

These are related to the upper third of the jugular vein, extending from the skull base to the inferior border of the hyoid bone. The anterior border of level II is the stylohyoid muscle, and the posterior border is the posterior border of the sternocleidomastoid muscle. The spinal accessory nerve, which travels obliquely across this area, is used as a landmark to subdivide this group into IIb, the portion above and behind the nerve, and IIa, the part that lies anteroinferiorly and closer to the internal jugular vein.

The nodes in level II are at greatest risk of harboring metastasis from cancers that arise from the oral cavity, nasal cavity, nasopharynx, oropharynx, hypopharynx, larynx, and parotid gland.

Middle jugular nodes (Level III) nodes

These are located between the hyoid superiorly and a horizontal plane defined by the inferior border of the cricoid cartilage. The sternothyroid muscle marks the anterior limit of level III, and the posterior border of the sternocleidomastoid muscle is the posterior border. Level III most commonly receives metastasis from cancers that originate in the oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx.

Inferior jugular nodes (Level IV)

These nodes refer to the group of nodes related to the lower third of the jugular vein. These nodes are located between the inferior border of the cricoid cartilage and the clavicle, and, like level III, the anterior boundary is the sternothyroid muscle, and the posterior border is the posterior border of the sternocleidomastoid muscle. The nodes of level IV commonly harbor metastasis from cancer that originates in the larynx, hypopharynx, thyroid, and cervical esophagus.

Posterior triangle group (Level V)

These nodes refer to the lymph nodes located in the posterior triangle of the neck. These include the spinal accessory, transverse cervical, and supraclavicular group of nodes. Level V is bound anteriorly by the posterior border of the sternocleidomastoid muscle and posteriorly by the anterior border of the trapezius muscle. Level V extends from the apex of the convergence of the sternocleidomastoid and trapezius muscle superiorly to the clavicle inferiorly. This level is subdivided by a plane defined by the inferior border of the cricoid cartilage into level Va superiorly and level Vb inferiorly. Level Va contains the nodes associated with the spinal accessory nerve, and level Vb contains the transverse cervical and supraclavicular nodes. The posterior triangle nodes are at greatest risk for harboring metastasis from cancers that arise in the nasopharynx, oropharynx, and skin of the posterior scalp and neck. The anterior, or central, compartment of the neck, located between the carotid arteries of the 2 sides, is rich in lymphatics that drain the thyroid gland, subglottic larynx, cervical trachea, hypopharynx, and cervical esophagus. Lymph nodes in this compartment are located in the tracheoesophageal groove (paratracheal nodes), in front of the trachea (pretracheal nodes), around the thyroid gland (perithyroidal nodes), and on the cricothyroid membrane (precricoid or Delphian node). Lymph nodes in the central compartment are not routinely excised in radical neck dissection; most commonly, they are removed during surgery for thyroid, laryngeal, and hypopharyngeal cancer. This group of nodes, although not

included in the original Memorial Sloan Kettering classification, is referred to as level VI. [9]

Probable Source of Nodal Metastasis

Submandibular/submental nodes: Oral cavity, submandibular gland.

Upper jugulodigastric nodes: Nasopharynx, oropharynx, parotid, supraglottic larynx.

Middle jugular nodes: Oropharynx, hypopharynx, supraglottic larynx.

Inferior jugular nodes: Subglottic larynx, hypopharynx, esophagus, thyroid.

Posterior triangle nodes: Nasopharynx, oropharynx.

Anterior compartment: Thyroid, larynx, lung.

Bilateral nodes are common with cancers of soft palate, tongue, epiglottis, and nasopharynx.

Pathological considerations

The approximately 600 lymph nodes in the body are strategically located along the course of lymphatics, which permits them to filter lymphatic fluid and encounter potential pathogens. The lymph nodes are populated predominantly by macrophages, dendritic cells, B lymphocytes , and T lymphocytes, which function together as a part of the normal immune response to microorganisms and foreign proteins. Swelling of lymph nodes induced by lymphocyte proliferation is a

normal response to antigen stimulation . Because children and adolescents are frequently exposed to new antigens, they commonly have enlarged nodes. Soft, flat nodes (<1 cm in diameter) often are palpable in the neck and axilla of healthy individuals , especially in children , and inguinal nodes upto 1 to 2 cm are generally normal in adults.The term lymphadenopathy refers to nodes that are abnormal in size, character (consistency), or number. Lymphadenopathy is "generalized" if nodes in two or more noncontiguous areas are involved and "localized" if just one area (or two contiguous areas) is involved. Generalized lymphadenopathy usually indicates systemic disease. In the primary care setting about 75% of patients with enlarged nodes present with localized lymphadenopathy. Lymph nodes themselves are seldom the primary site of a bacterial infection, but swollen nodes typically are present in an area that receives drainage from an infected site. [4]Lymph nodes, in conjunction with the spleen, tonsils, adenoids, and Peyer patches, are highly organized centers of immune cells that filter antigen from the extracellular fluid. Directly interior to the fibrous capsule is the subcapsular sinus. This allows lymph, an ultrafiltrate of blood, to traverse from the afferent lymph vessels, through the sinuses, and out the efferent vessels. In addition to supplying lymph with a channel for lymph flow, the sinuses are studded with macrophages, which remove 99% of all delivered antigens. Interior to the subcapsular sinus is the cortex containing primary follicles, secondary follicles, and the interfollicular zone. Follicles within the cortex are major sites of B-cell proliferation, whereas the interfollicular zone is the site of antigen-dependent T-cell differentiation and proliferation. The deepest structure

within the lymph node is the medulla, consisting of cords of plasma cells and small B lymphocytes that are architecturally arranged near the sinuses to facilitate immunoglobulin secretion into the exiting lymph. The lymph node, with its high concentration of lymphocytes and antigen-presenting cells, is an ideal organ for the delivery of antigen that gains access through the skin or gastrointestinal tract. Nodes have considerable capacity for growth and change. Lymph node size depends on the person's age, the location of the lymph node in the body, and antecedent immunological events. In neonates, lymph nodes are barely perceptible. Thereafter begins a progressive increase in total lymph node mass until later childhood. Lymph node atrophy begins during adolescence and continues throughout life.

Pathophysiology:

Most lymphadenopathy in children is due to benign self-limited disease because self-limited viral or bacterial infections are the most common causes. Lymphadenopathy can be caused by an increase in normal lymphocytes and macrophages during a response to an antigen (eg, viral illness), nodal infiltration by inflammatory cells in response to an infection in the nodes themselves (lymphadenitis), proliferation of neoplastic lymphocytes or macrophages (lymphoma), or infiltration of nodes by metabolite-laden macrophages in storage diseases (Gaucher disease).

Frequency:

The precise incidence of lymphadenopathy is not known. Lymphadenopathy is one of the most common clinical problems encountered in pediatrics. It is often difficult to determine whether adenopathy is simply a normal response to frequent viral infections within an age group or if it is significant enough to consider more serious underlying disease. In Asia, common viral and bacterial infections are overwhelmingly the most common cause of adenopathy. Infectious mononucleosis and cytomegalovirus (CMV) are important etiologies, but adenopathy is usually caused by common viral upper respiratory tract infections. Localized lymphadenitis is most often caused by staphylococci and beta-hemolytic streptococci. Other infections, such as HIV, malignancies, and autoimmune diseases, are less common causes of adenopathy in Asia. Infections that are commonly observed in Asia and the developing countries are less commonly observed in United States. These include tuberculosis, typhoid fever, leishmaniasis, trypanosomiasis, schistosomiasis, filariasis, and fungal infections. HIV infections must be considered strongly in areas of high incidence in the United States.

Mortality/Morbidity:

Mortality and serious morbidity caused by adenopathy are unusual given the common infectious etiologies. HIV is an uncommon cause of adenopathy, but its associated mortality requires consideration. Malignancies, such as squamous

cell carcinomas, adenocarcinomas, leukemia, and lymphomas, are the primary causes of mortality. Significant morbidity and mortality are also associated with rare serious infections, autoimmune disorders (eg, juvenile rheumatoid arthritis, systemic lupus erythematosus), histiocytoses, and storage diseases.

Race:

Race is not a major factor in most disorders associated with lymphadenopathy.

Sex:

Sex is not a major factor associated with lymphadenopathy.

Age:

Adenopathy is most common in young children whose immune systems are responding more frequently to newly encountered infections. Adenopathy is uncommon in the neonate who usually has not had significant exposure to infectious etiologies and in whom other disorders associated with lymphadenopathy are rare. The peak prevalence of leukemia is in children younger than 10 years, whereas Hodgkin disease is observed more often in adolescents. [10]

Cervical Lymphadenopathy

Cervical nodes drain the tongue, external ear, parotid gland, and deeper structures of the neck, including the larynx, thyroid, and trachea. Inflammation or direct infection of these areas causes subsequent engorgement and hyperplasia of their respective node groups. Adenopathy is most common in cervical nodes in children and usually is related to infectious etiologies. Lymphadenopathy posterior to the sternocleidomastoid typically is a more ominous finding, with a higher risk of serious underlying disease.

Infectious causes

Cervical adenopathy is a common feature of many viral infections. Infectious mononucleosis often manifests with posterior and anterior cervical adenopathy. Firm tender nodes that are not warm or erythematous characterize this lymph node enlargement. Other viral causes of cervical lymphadenopathy include adenovirus, herpesvirus, coxsackievirus, and CMV. In herpes gingivostomatitis, impressive submandibular and submental adenopathy reflects the amount of oral involvement. Bacterial infections cause cervical adenopathy by causing the draining nodes to respond to local infection or by the infection localizing within the node itself as a lymphadenitis. Bacterial infection often results in enlarged lymph nodes that are warm, erythematous, and tender. Localized cervical lymphadenitis typically begins as enlarged, tender, and then fluctuant nodes. The

appropriate management of a suppurative lymph node includes both antibiotics and incision and drainage. Antibiotic therapy should always include coverage for Staphylococcus aureus and Streptococcus pyogenes. In patients with cervical adenopathy, any history of recent or ongoing sore throat or ear pain and examination of the oropharynx, paying special attention to the posterior pharynx and the dentition are important . The classic manifestation of Group A streptococcal pharyngitis is sore throat, fever, and anterior cervical lymphadenopathy. Other streptococcal infections causing cervical adenopathy include otitis media, impetigo, and cellulitis. Atypical mycobacteria cause subacute cervical lymphadenitis with nodes that are large and indurated but not tender. The only definitive cure is removal of the infected node. Mycobacterium tuberculosis may manifest with a suppurative lymph node identical to that of atypical mycobacterium. Intradermal skin testing may be equivocal. Catscratch disease, caused by *Bartonella henselae,* presents with subacute lymphadenopathy often in the cervical region. The disease develops after the infected pet (most likely a kitten) inoculates the host, usually through a scratch. Approximately 30 days later, fever, headache, and malaise develop, along with adenopathy that often is tender. Several lymph node chains may be involved. Suppurative adenopathy occurs in 10-35% of patients. Antibiotic therapy has not been shown to shorten the course.

Malignant metastasis to cervical lymph nodes

Cancers of the oropharynx, squamous cell carcinoma accounts for the most frequent metastasis to cervical lymph nodes, mostly occupying the submandibular/submental nodes and upper jugulodigastric lymph nodes.[11] Other studies done by W. Giridharan et al also favours this finding as they report most common tumor to metastasize to cervical lymph nodes were squamous cell carcinoma (73%) , followed by lymphomas (28%) and adenocarcinoma (27%). [12] Mostafa et al [13] also reports squamous cell carcinoma to be the most frequent metastasis to cervical lymph node. This is not surprising as more than 90% of head and neck tumors comprise of squamous cell carcinoma.[14] Studies done by Nada A Alwan [15] and Bezabiah [16] report that lymphomas constituted the main pathology in malignant involvement (26%), while metastatic lesions formed 16.7% and leukemias 2%.

Noninfectious and infectious etiologies in children

Malignant childhood tumors develop in the head and neck region in 27% of cases. In the first 6 years of life, neuroblastoma, leukemia, non-Hodgkin lymphoma, and rhabdomyosarcoma (in order of decreasing frequency) are most common in the head and neck region. In children older than 6 years, Hodgkin disease and non-Hodgkin lymphoma both predominate. Children with Hodgkin disease present with cervical adenopathy in 80-90% of cases as opposed to 40% of those with non-Hodgkin lymphoma.

Kawasaki disease is an important cause of cervical adenopathy. These children have fever for at least 5 days, and cervical lymphadenopathy is one of the 5 diagnostic criteria (of which 4 are necessary establish the diagnosis). Submaxillary and submental lymphadenopathy: These nodes drain the teeth, tongue, gums, and buccal mucosa. Their enlargement usually is the result of localized infection, such as pharyngitis, herpetic gingivostomatitis, and dental abscess.

Occipital lymphadenopathy:

Occipital nodes drain the posterior scalp. These nodes are palpable in 5% of healthy children. Common etiologies of occipital lymphadenopathy include tinea capitis, seborrheic dermatitis, insect bites, orbital cellulitis, and pediculosis. Viral etiologies include rubella and roseola infantum. Uncommonly, occipital lymphadenopathy may be noted after enucleation of the eye for retinoblastoma.

Preauricular lymphadenopathy:

Preauricular nodes drain the conjunctivae, skin of the cheek, eyelids, and temporal region of the scalp and rarely are palpable in healthy children. The oculoglandular syndrome consists of severe conjunctivitis, corneal ulceration, eyelid edema, and ipsilateral preauricular lymphadenopathy. Chlamydia trachomatis and adenovirus can cause this syndrome.

Supraclavicular lymphadenopathy

Supraclavicular nodes drain the head, neck, arms, superficial thorax, lungs, mediastinum, and abdomen. Left supraclavicular nodes also reflect intra-abdominal drainage and enlarge in response to malignancies in that region. This is particularly true when adenopathy in this region occurs in the absence of other cervical adenopathy.

Right supraclavicular nodes drain the lung and mediastinum and are typically enlarged with intrathoracic lesions.

Serious underlying disease is frequent in children with supraclavicular adenopathy and always merits further evaluation. The potential for malignancy necessitates peripheral blood counts, skin testing for tuberculosis, and chemical studies, including uric acid, lactate dehydrogenase, calcium (Ca), phosphorus (P), and renal and hepatic function studies. Chest radiography and possibly computerized tomography are indicated. Several important infections may occur with supraclavicular adenopathy,including tuberculosis, histoplasmosis, and coccidioidomycosis. Early lymph node biopsy should be considered in children with supraclavicular adenopathy.[10]

Prognosis according to level of lymph node metastasis

Studies done by Jones AS et al reports that 5 year survival of metastatic squamous cell carcinoma to the cervical lymph nodes were 51% and survival fell

from increasing to decreasing node level (submandibular/submental to posterior cervical group), being 37% for submandibular lymph nodes , 32% for deep cervical lymph nodes , and 25% for lower deep cervical lymph nodes. The 18 month survival for supraclavicular and posterior triangle nodes were 21%. Multivariate analysis confirmed that as the level of the nodes fell from submandibular region to supraclavicular region the prognosis worsened. Upper jugulodigastric cervical lymph nodes were most commonly involved with regards to all primary sites and found in 69% of all neck node metastasis. [17] Ipsilateral metastasis to cervical lymph nodes were seen as the common presentation to submandibular/submental nodes and upper jugulodigastric lymph nodes, and are not associated with prognosis of the patient.[18,19]

Literature of Fine needle aspiration cytology

FNA for cytologic evaluation of a neck mass was first reported by Kun in 1847. However, the procedure did not gain wide acceptance in medicine at that time. In the 1930s, Memorial Sloan Kettering rediscovered the utility of needle biopsy of head and neck masses. The use of large-bore needles at that time led to frequent complications, 1 of which was occasional seeding of the tumor along the biopsy tract. The frequent morbidity associated with this procedure preventedwidespread acceptance of this technique in other centers of America. A resurgence of FNA occurred in the 1950s, led by physicians in Sweden. FNA was commonly used for cytologic examination of metastatic lesions in the neck with excellent results. Since then, FNA of solitary neck masses has become a

well-accepted, safe, and cost-effective procedure in the diagnosis of neck masses.[20] Countries with the most developed aspiration biopsy are Sweden, Slovenia and India. At Karolinska hospital (Stockholm, Sweden), the annual volume average seven thousand aspirates; at Institute of Oncology (Ljubljana, Slovenia) ten thousand.[21] FNA is a simple office procedure requiring a few minutes to complete. If cytotechnologists and pathologists are available, diagnosis can often be made immediately.

FNA has several advantages over excisional biopsy. In today's economic environment, cost savings is an important consideration in medicine. FNA is also more convenient for patients and their families. The procedure requires only an office visit with minimal loss of time from work. On the other hand, excisional biopsy often requires time off from work, preoperative blood tests, and often, radiographic and cardiac testing. Furthermore, surgery exposes patients to the risks of anesthesia, postoperative infection, and the possibility of tumor seeding. A percentage of patients may require overnight admission to the hospital and extra time from work. However FNA for cervical lymph nodes has several limitations. Failure to establish an accurate diagnosis may be because of sampling error. In these circumstances, repeat aspiration is suggested, and excisional biopsy may be considered. Personnel responsible for handling, processing (experienced cytotechnologist), and reading (cytopathologist) of FNA samples must be well trained. Interobserver variability must be minimized.

No medical procedure is without risks. Due to the small size of the needle, the chance of spreading a cancer or finding cancer in the needle path is very small. Other complications are rare; the most common is bleeding. If bleeding occurs at all, it is generally seen as a small bruise. Patients who take aspirin, or blood thinners, are more at risk to bleed. However, the risk is minimal. Infection is rarely seen.[22]

Fine needle aspiration cytology in cervical lymphadenopathy

Fine needle aspiration cytology in the diagnosis of cervical lymphadenopathy is found to be an inexpensive, useful tool with high diagnostic accuracy. Mondal A et al found a diagnostic accuracy of 100% for benign conditions of the lymph nodes like tuberculous lymphadenitis [23] and pyogenic lymphadenitis, giving an overall accuracy of 96.2%. [24] Similar observations were made by Prasad et al having an overall accuracy of 91.5%. [25] Similarly malignant metastasis to the cervical lymph node had a high diagnostic accuracy as given by Shaha et al [26] and LeeJY [27] et al, who reported 96% and 95.7% respectively. Accuracy for malignant tumors with correct diagnosis being made in case of metastatic squamous cell carcinomas, adenocarcinomas, lymphomas and thyroid malignancies. Lymphomas have a sensitivity of 82.5%, and benign conditions have a sensitivity of 97.3%. Gupta et al [28] reports metastatic carcinoma to have a higher diagnostic value , however diagnosis of reactive hyperplasia and Non

Hodgkin's lymphoma could be problematic. Metastatic thyroid malignancies have an accuracy rate of 79.1%. [29] Of these papillary carcinomas constituted the majority of conditions. [30] Most of the thyroid malignancies like papillary carcinoma, Hurthle cell carcinoma, Anaplastic carcinoma did not produce much discrepancies in obtaining the accurate diagnosis. To obtain a diagnosis of metastatic small cell carcinoma and Non Hodgkins Lymphoma could be challenging. Studies conducted by De Las et al [31] found out the presence of evenly dispersed fine granular chromatin, paranclear blue inclusions and nuclear fragments were statistically significant in differentiating small cell carcinoma from Non-Hodgkin's lymphoma. Diagnostic discrepancies can occur when differentiating anaplastic large cell lymphoma, undifferentiated carcinoma and some cases of Hodgkin's lymphoma.[32]Immunophenotyping can be of value in these instances. Supraclavicular lymph nodes were most likely to be involved by malignant metastasis. Malignancy was present in 55% of the supraclavicular lymph nodes by studies done by Ellison et al [33] and 85% by Steel et al [34], and their primary being mostly from lungs, breast and cervix. Sensitivity of fine needle aspiration was seen to be 97% and specificity 98%. FNAC in children and adolescents were compared in a study done by Ponder et al [35] who obtained FNAC samples from children <10 years and adolescents 4.7% of inconclusive results were reported in the younger age group, and few inconclusive results in the older age group. Majority of conditions included benign reactive conditions than malignant tumors and FNAC was found to be a reliable tool in diagnosing cervical lymphadenopathy in children. FNAC in patients with acquired

immunodeficiency syndrome [36] with cervical lymphadenopathy and homosexuals [37] were found to give prompt diagnosis and rapid initiation of treatment which led to symptomatic improvement. Of the conditions that affect the cervical lymph node, tuberculous lymphadenitis were found to be more prevalent in low socioeconomic groups, such as parts of India. [38] However two studies done in Middle east [39, 40], such as Kingdom of Saudi Arabia shows Tuberculous lymphadenitis as more prevalent. FNAC showed a sensitivity of 76.9% in study done by Hsu C et al. [41]FNAC is therefore reliable, cheap, cost-effective as well as rapid and is followed by fewer complications as compared to excision biopsy.

RESULT

Results:

A total of 1859 fine needle aspirations were done in the Dept of Pathology during Nov 2005 to Nov 2006. Among them, 299 cases were from cervical lymph nodes. Subsequent biopsy following FNAC were done in 101 cases, the remaining 198 cases biopsy were not available.

Figure : 1: Total results of FNAC in 1 year period

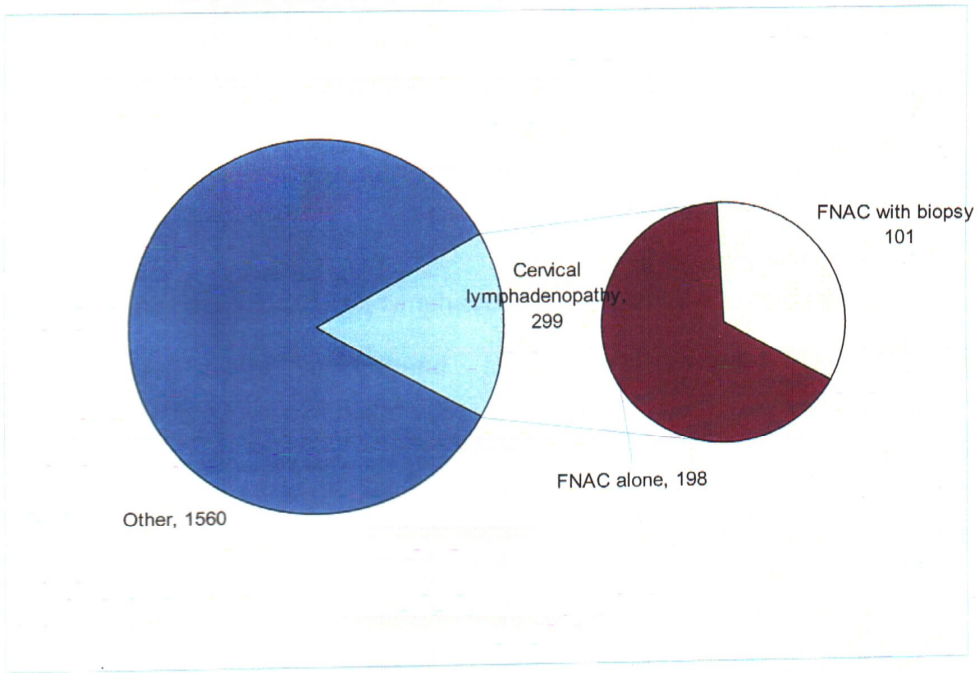
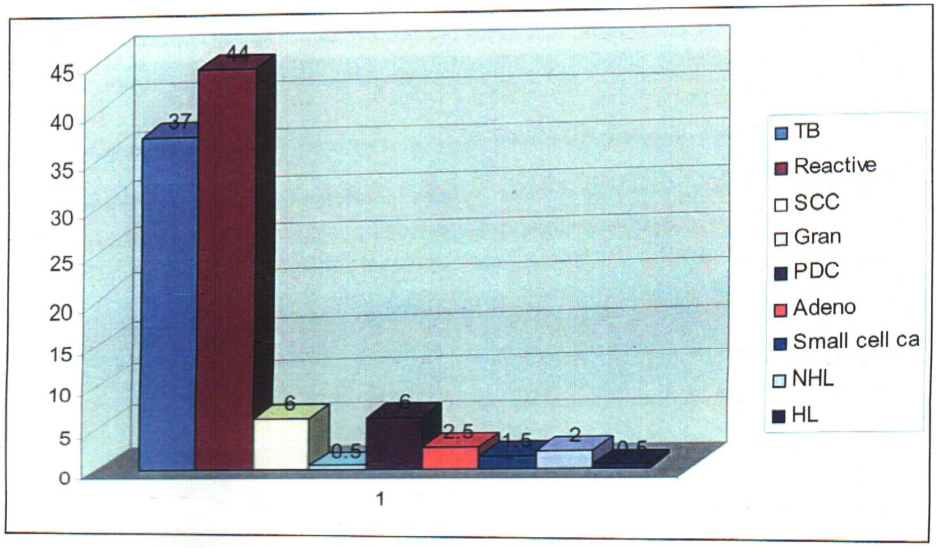
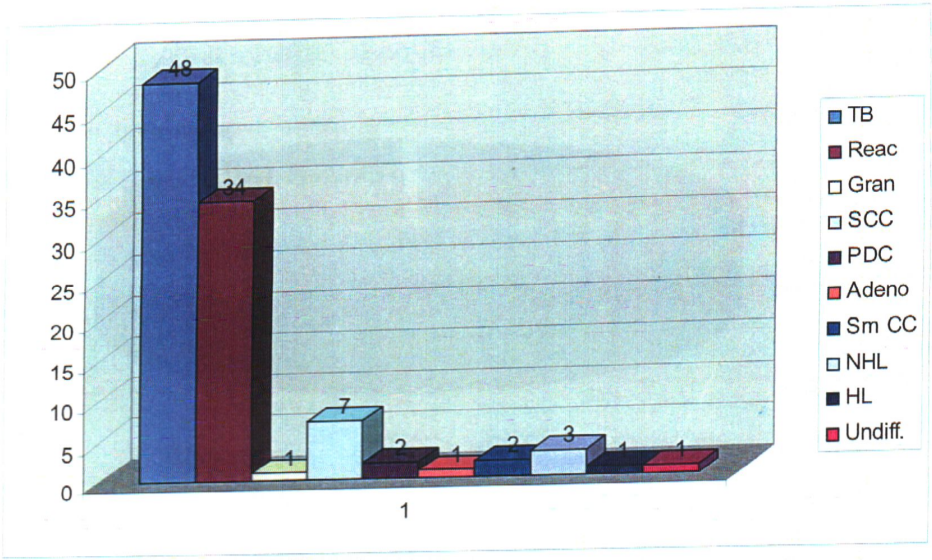


Figure 2: Frequency of diseases causing cervical lymphadenopathy diagnosed by FNAC:



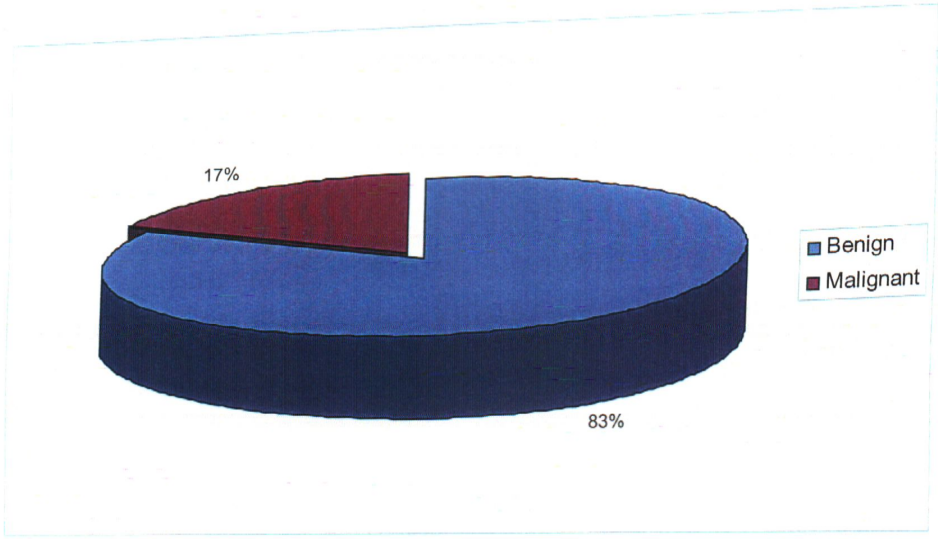
A total of 299 cases of cervical lymphadenopathy were diagnosed by FNAC. Reactive lymphadenitis was found to be more prevalent (44%) than TB lymphadenitis (37%).

Figure 3: Frequency of different diseases of cervical lymphadenopathy diagnosed by excisional biopsy:



Of the benign lesions Tuberculous lymphadenitis was the commonest (48 %), followed by reactive lymphadenitis and granulomatous lymphadenitis. Of the malignant conditions that metastasises to the cervical lymph node, squamous cell carcinoma was found to be the commonest (7%). Of the lymphomas, incidence of Non-Hodgkin's lymphoma were seen to be more than that of Hodgkin's lymphoma.

Figure 4: Distribution of benign and malignant conditions causing cervical lymphadenopathy diagnosed by biopsy:



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In this study majority of the conditions were benign lesions comprising 83%. Malignant conditions constitute 17%.

Patients age ranged from 4 years to 68 years. The largest number of patients were in the age group 20-39, followed by age group1-19. It was observed that largest number of benign conditions , such as TB lymphadenitis and reactive lymphadenitis occurred at the age below 40 years, and malignant metastasis to cervical lymph node occurred in the age above 40 years.

Table 1: Age distribution of patients presented with cervical lymphadenopathy (in benign and malignant conditions):

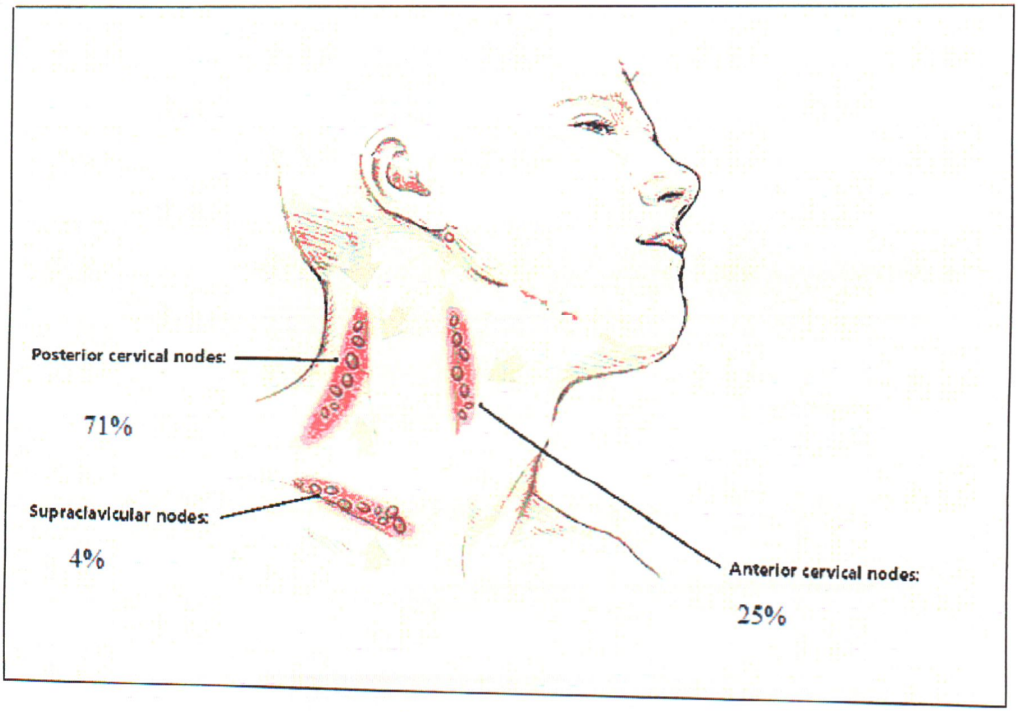
Age	Benign	Malignant	Total/Percentage
1-19 yrs	32	1	33 (32.60%)
20-39 yrs	44	0	44 (43.6%)
40-59 yrs	6	8	14 (13.9%)
60-79 yrs	2	8	10 (9.90%)
Total/Percentage	84 (83.2%)	17 (16.8%)	101 (100%)

Table 2: Sex distribution of patients presented with cervical lymphadenopathy

Sex	Benign	Malignant	Total/Percentage
Male	39	10	49 (48.5%)
Female	45	7	52 (51.5%)
Total/Percentage	84 (83.2%)	17 (16.8%)	101 (100%)

Male patients comprise of 48.5%, while female patients comprise of 51.5%, giving a male to female ratio of 1:1.

Figure 5: Sites of lymph node involvement:



Most of the patients presented with posterior cervical lymph node enlargement (71%), either single or multiple, followed by anterior cervical lymph node enlargement (25%) and only 4% presented with supraclavicular lymph node enlargement.

Table 3 : Site and side of lymph node involvement:

	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		
	Single	Multiple	Single	Multiple	Single	Multiple	Total/Percentage
Right	5	3	20	10	2	1	41 (40.6%)
Left	2	4	18	6	1	0	31 (30.7%)
Bilateral	0	12	0	17	0	0	29 (28.7%)
Total	7 (6.9%)	19 (18.8%)	38 (37.6%)	33 (32.7%)	3 (3.0%)	1 (1.0%)	101 (100%)

Most of the affected lymph nodes were present on the right side (40.6%), followed by left side (30.6%). Multiple, bilateral lymph nodes were enlarged in 28.7% patients.

The posterior group of lymph nodes were the most commonly affected group of lymph nodes on the right (30), left side (24), and even bilaterally (17).

Table 4: Single lymph node enlargement in different sites and sides

Single LN enlargement							
	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		Total/Percentage
Disease	Right	Left	Right	Left	Right	Left	
TB LN	0	0	7	5	0	0	12 (25%)
Reac LN	1	0	13	11	0	0	25 (52.1%)
SCC	4	0	0	0	2	0	6 (12.5%)
SmCC	0	1	0	1	0	0	2 (4.2%)
PDC	0	1	0	1	0	0	2 (4.2%)
Adenoca	0	0	0	0	0	1	1 (2.0%)
Total	5 (10.4%)	2 (4.2%)	20 (41.7%)	18 (37.5%)	2 (4.2%)	1 (2.0%)	48 (100%)

Table 5: Multiple unilateral lymph node enlargement in different sites and sides

Multiple LN enlargement							
	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		Total/Percentage
Disease	Right	Left	Right	Left	Right	Left	
TB LN	2	2	9	5	0	0	18 (53.0%)
Reac LN	1	1	1	11	1	0	15 (44.1%)
SCC	0	1	0	0	0	0	1 (2.9%)
Total/ Percentage	3 (8.8%)	4 (11.7%)	10 (29.4%)	16 (47.1%)	1 (3.0%)	0 (0%)	34 (100%)

Reactive lymphadenitis was seen as the most frequent disease to present as

single lymph node enlargement, irrespective of the side of involvement. Whereas when multiple lymph node enlargement was encountered, TB lymphadenitis was seen to be the most frequent condition.

Metastatic carcinomas were seen to involve all three groups of lymph nodes.

Table 6: Bilateral lymph node enlargement

	Bilateral/Multiple LN enlargement		
Disease	Anterior cervical LN	Posterior cervical LN	Total/Percentage
Tuberculous lymphadenitis	4	15	19 (65.5%)
Reactive lymphadenitis	3	1	4 (14.0%)
Granulomatous lymphadenitis	0	1	1 (3.4%)
Non-Hodgkin's lymphoma	3	0	3 (10.3%)
Hodgkin's lymphoma	1	0	1 (3.4%)
Undifferentiated carcinoma	1	0	1 (3.4%)
Total/ Percentage	12 (41.4%)	17 (58.6%)	29 (100%)

TB lymphadenitis was the most common cause of bilateral multiple lymphadenopathy, followed by reactive lymphadenitis and NHL.

Table 7: Duration of lymphadenopathy:

Disease	1-3 months	3-6 months	6-12 months	>12 months	Total/Percentage
TB LN	33	13	2	1	49 (48.5%)
Reactive LN	34	0	0	0	34 (33.6%)
Granulomatous LN	1	0	0	0	1 (1.0%)
SCC	0	1	6	0	7 (6.9%)
PDC	0	0	2	0	2 (2.0%)
Adenoca	0	0	1	0	1 (1.0%)
SmCC	0	2	0	0	2 (2.0%)
NHL	3	0	0	0	3 (3.0%)
HL	1	0	0	0	1 (1.0%)
Undiff ca	1	0	0	0	1 (1.0)
Total/Percentage	73 (72.3%)	16 (15.8%)	11(10.9%)	1 (1.0%)	101 (100%)

Of the benign conditions, most of the patients of TB (33%) and reactive lymphadenitis (34%) presented with lymph node enlargement during their first 3 months. TB lymphadenitis was also seen to have a longer duration (3-12 months) in 15% patients.

Most of the malignant conditions, in this study presented with lymph node enlargement, at 6-12 months time period, however lymphomas such as NHL, Undifferentiated carcinoma and Hodgkin's presented in the first 3 months period.

Table 8: Size of lymph nodes:

Disease	<1cm	1-2cm	3-4cm	Total/Percentage
TB LN	0	23	26	49 (48.5%)
Reactive LN	1	31	2	34 (33.6%)
Granulomatous LN	0	1	0	1 (1.0%)
SCC	0	0	7	7 (6.9%)
PDC	0	0	2	2 (2.0%)
Adenoca	0	0	1	1 (1.0%)
SmCC	0	2	0	2 (2.0%)
NHL	0	2	1	3 (3.0%)
HL	0	0	1	1 (1.0%)
Undiff ca	0	0	1	1 (1.0%)
Total/Percentage	1 (1.0%)	59 (58.4%)	41 (40.6%)	101 (100%)

Patients of the TB lymphadenitis presented with multiple matted firm lymph nodes of 3-4 cm in maximum dimension. Reactive lymphadenitis presented as firm, discrete, single lymph nodes of 1-2 cm in maximum dimension.

Malignant conditions presented with hard fixed lymph nodes of maximum dimension 3-4cm. Lymphomas had a rubbery architecture to the lymph nodes.

Table 9: Correlation of FNAC with histopathologic diagnosis in cervical lymphadenopathy :

	FNAC	Histopathology									
		TB	Reac	Gran	SCC	PDC	AdenoC	SmallCC	NHL	HL	UndifC
TB LN	44	44	0	0	0	0	0	0	0	0	0
Reac LN	35	1	34	0	0	0	0	0	0	0	0
Gran LN	5	4	0	1	0	0	0	0	0	0	0
SCC	7	0	0	0	7	0	0	0	0	0	0
PDC	2	0	0	0	0	2	0	0	0	0	0
AdenoC	1	0	0	0	0	0	1	0	0	0	0
SmCC	2	0	0	0	0	0	0	2	0	0	0
NHL	4	0	0	0	0	0	0	0	3	0	1
HL	1	0	0	0	0	0	0	0	0	1	0

It was seen that 44 of the TB lymphadenitis cases correlated correctly with histopathology. However, 4 cases of histopathologically diagnosed TB lymphadenitis were reported as granulomatous lymphadenitis by FNAC and 1 case of histopathologically diagnosed TB lymphadenitis were diagnosed as reactive lymphadenitis on FNAC. Granulomatous lymphadenitis were thus taken as true positives for TB lymphadenitis , and the one case which failed to diagnose TB lymphadenitis on FNAC was taken as a false negative for TB lymphadenitis .

For cases of Squamous cell carcinoma, adenocarcinoma , poorly differentiated carcinoma, small cell carcinoma, and Hodgkins' s lymphoma, all cases of FNAC and histopathology were correlated correctly. One case of Anaplastic large cell lymphoma (NHL) Diagnosed on FNAC was diagnosed as undifferentiated carcinoma on histopathology, giving a false negative result. There were no false positive cases.

Sensitivity and specificity of FNAC in this study:

It was found that sensitivity was 98% and specificity was 100%.

Positive predictive value: 100%

Negative predictive value: 99.7%

Table 10: Sensitivity and specificity of FNAC in diagnosing benign and malignant conditions:

	FNAC	false negative	HPE	Sensitivity	Specificity
Benign	n=43	n=1	n=44	98.80%	100%
Malignant	n=16	n=1	n=17	94%	100%
Total	n=99	n=2	n=101		

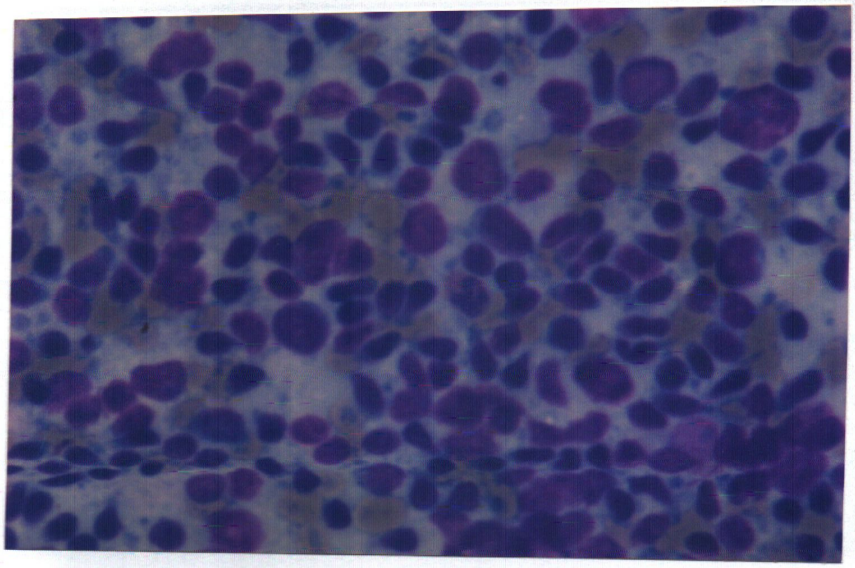


Fig 1: Reactive lymphadenitis, FNAC (Giemsa stain, x 400)

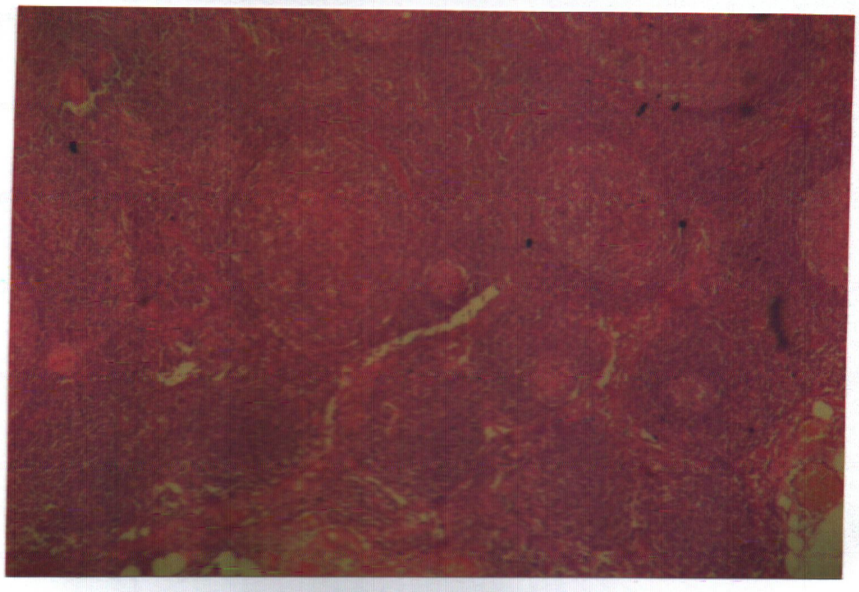


Fig 2: Reactive lymphadenitis, tissue section (H & E stain, x 100)

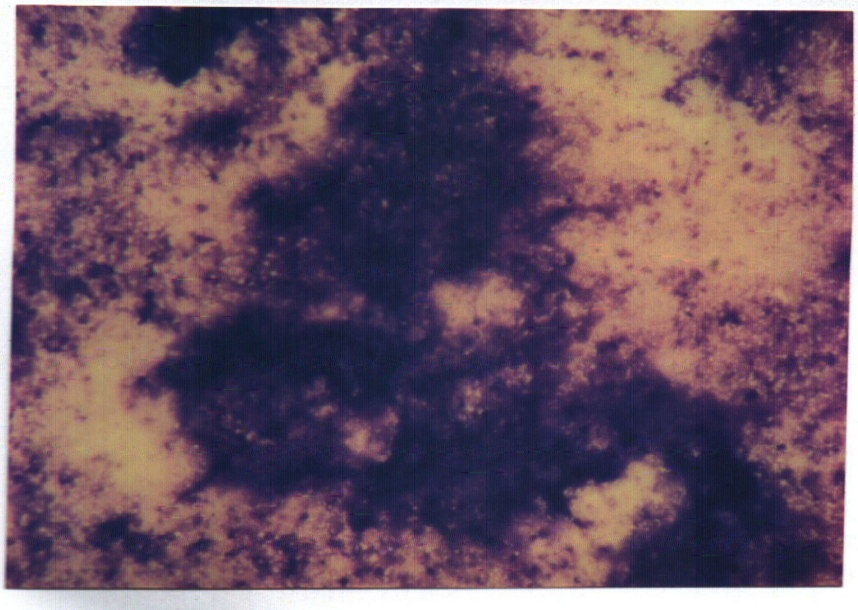


Fig 3: Tuberculous lymphadenitis, FNAC (Giemsa stain, x 100)

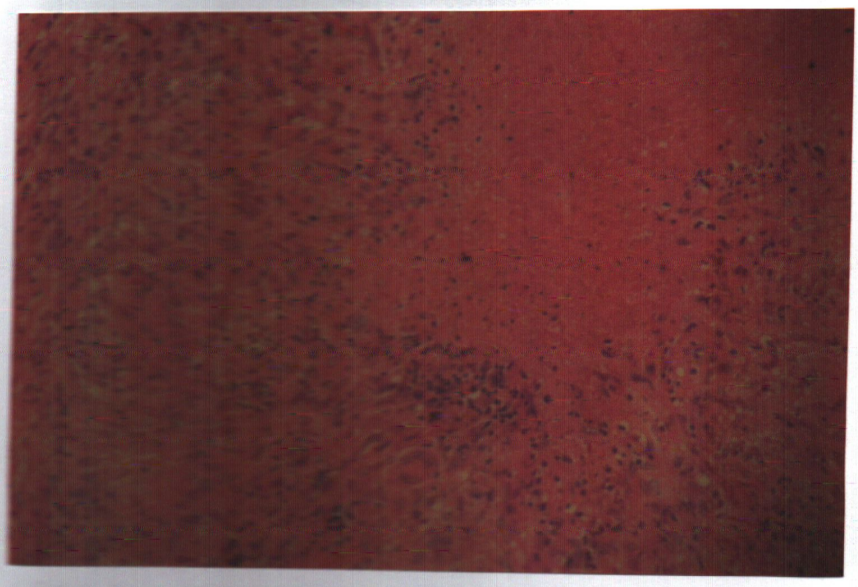


Fig 4: Tuberculous lymphadenitis, tissue section (H & E stain, x 100)

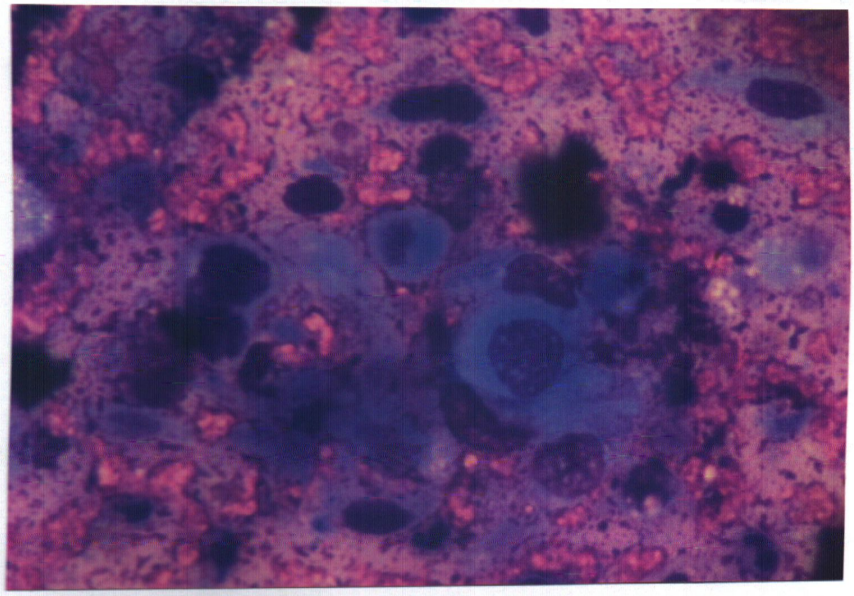


Fig 5: Metastatic squamous cell carcinoma, FNAC (Giemsa stain, x 400)

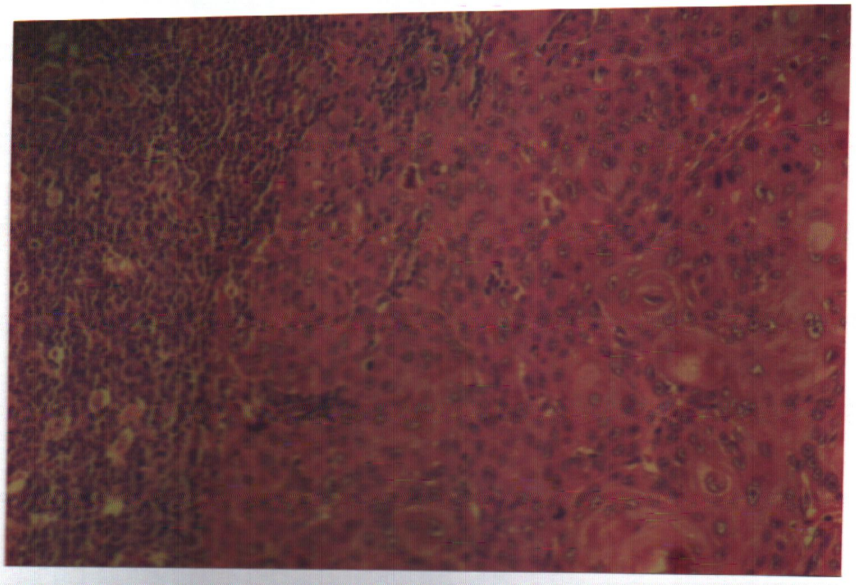


Fig 6: Metastatic squamous cell carcinoma, tissue section (H & E stain, x100)

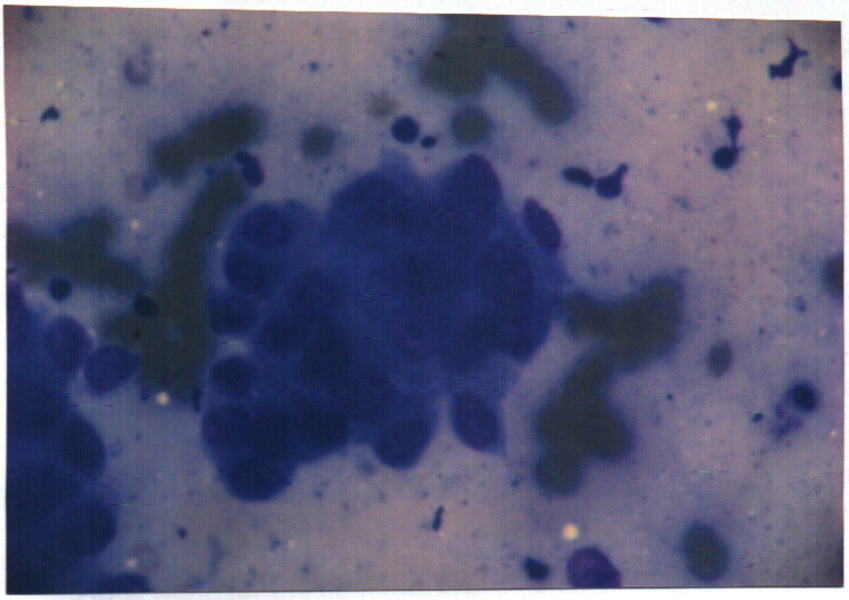


Fig 7. Metastatic adenocarcinoma, FNAC (Giemsa stain, x 400)

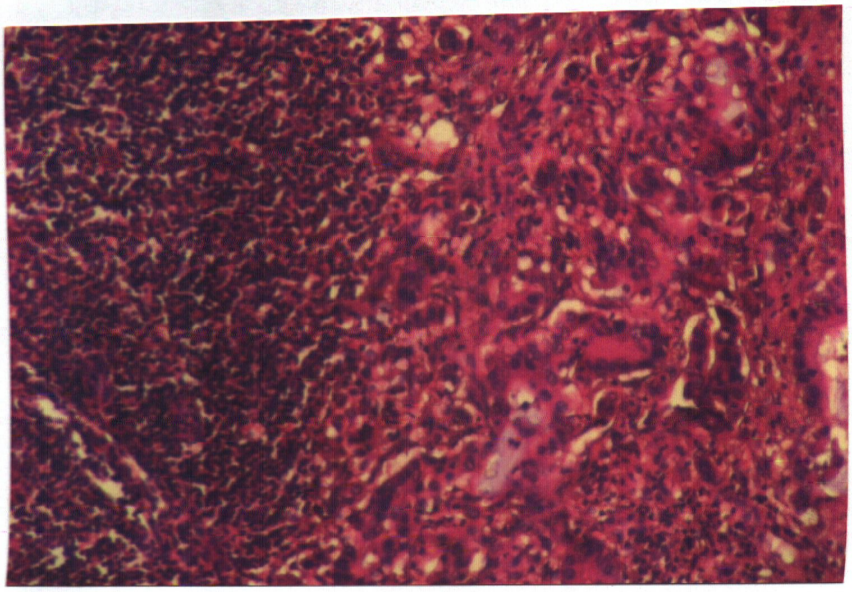


Fig 8: Metastatic adenocarcinoma , tissue section (H & E stain, x400)

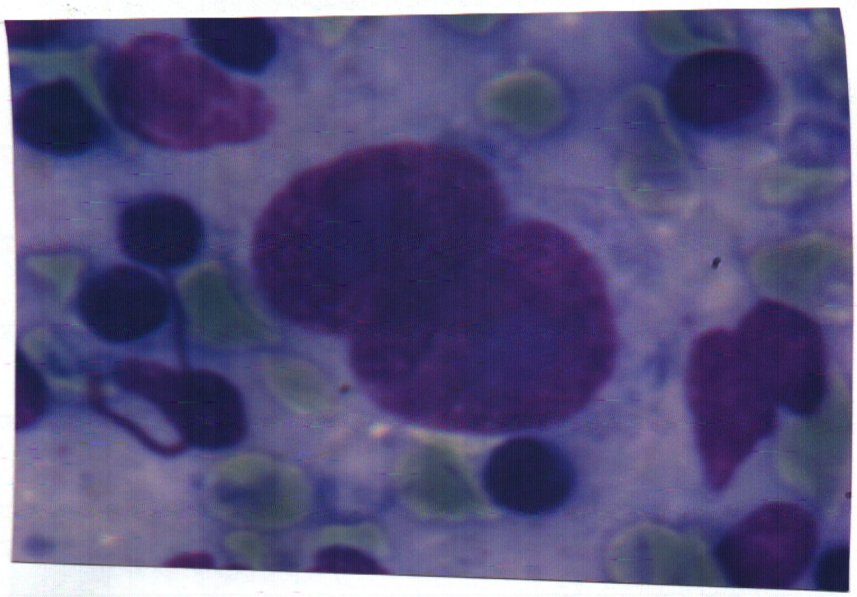


Fig 9: Hodgkin's lymphoma, FNAC (Giemsa stain, x 1000)

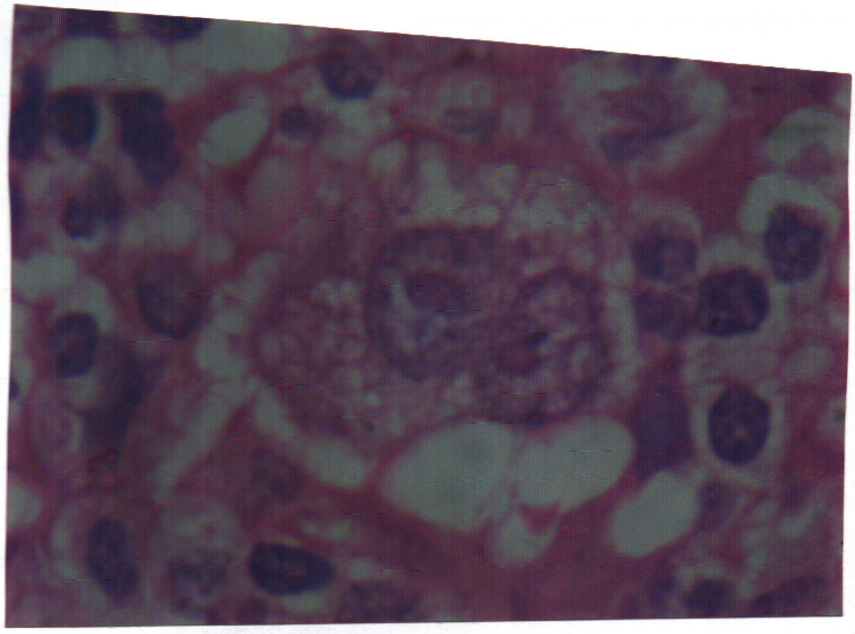


Fig 10: Hodgkin's lymphoma, tissue section (H & E stain, x1000)

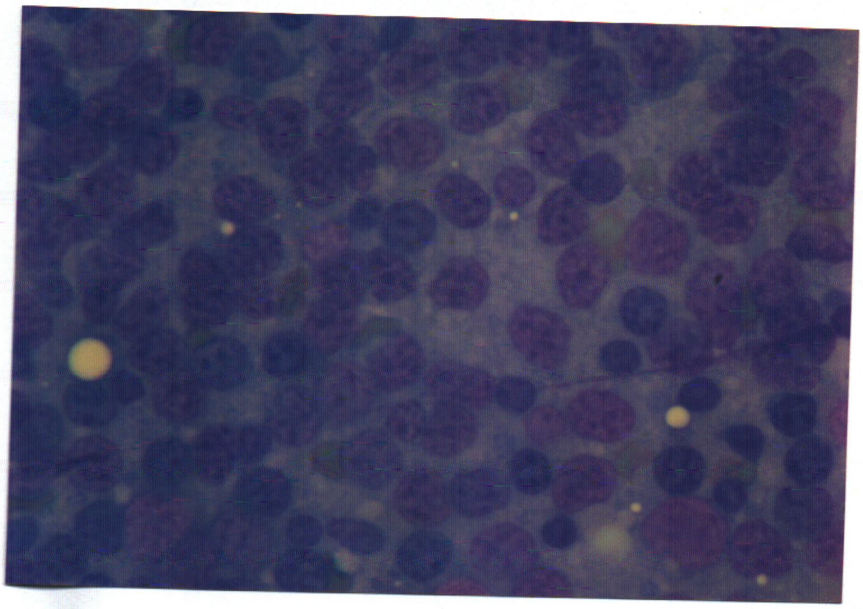


Fig 11: Non-Hodgkin's lymphoma, FNAC (Giemsa stain, x 400)

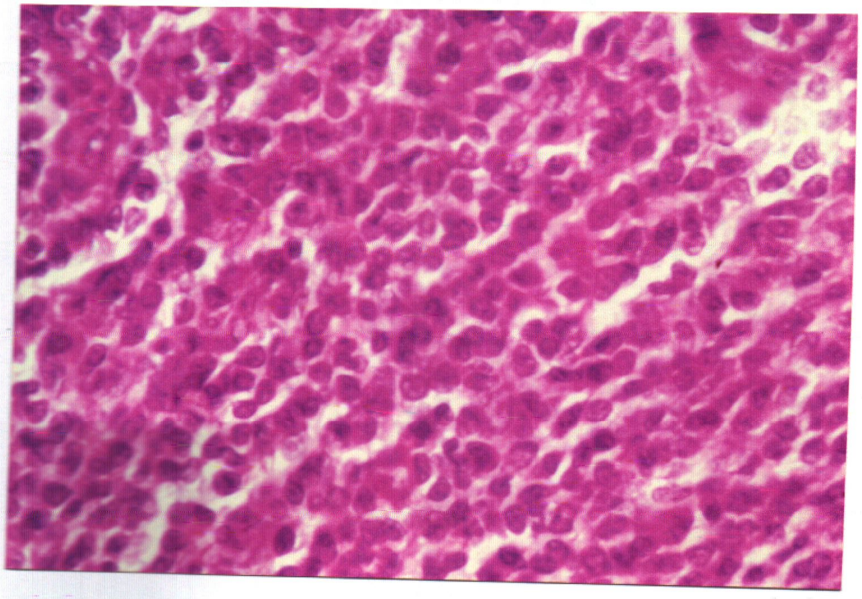


Fig 12: Non-Hodgkin's lymphoma, tissue section (H & E stain, x400)

DISCUSSION

Discussion:

The use of fine needle aspiration cytology (FNAC) in the investigation of lymphadenopathy has become an acceptable and widely practiced minimally invasive technique, which is safe, simple, rapid and relatively pain- free. FNAC is highly cost effective and accurate as a first line investigative technique. In this study, FNAC of cervical lymph nodes were obtained from 101 patients who presented with cervical lymphadenopathy. Cytological findings were analysed in correspondence to histopathological diagnosis of the same excised lymph nodes. Benign lesions were found to constitute of 83% of the enlarged lymph nodes, of which majority were tuberculous lymphadenitis, which constitute 48%, followed by reactive lymphadenitis, which constitute 34%, followed by one case of granulomatous lymphadenitis. These findings correlate with studies done by Nada. A. Alwan et al and Kiery J at el [42], who also reported benign conditions comprising majority of cervical lymphadenopathy 55.3% and 49.5% respectively. Taking in consideration the 299 fine needle aspiration cytology aspirations of cervical lymphadenopathies done through the whole year, reactive lymphadenitis constituted the majority of cases. This goes in accordance with study done by Nada et al. A possible explanation for this is that the study was performed in the Middle east where a high socioeconomic class population resides, where tuberculosis is not as prevalent as the Asian population. But however when the 101 cases were taken which followed biopsy, tuberculous lymphadenitis constituted majority of cases. Kiery J et al reported tuberculous lymphadenitis to be more common than that of reactive lymphadenitis. Malignant metastasis to the

cervical lymph nodes were seen to be more common than the primary neoplasms of the lymph node. This finding also goes in accordance with study done by Keiry J et al who reported that malignant metastasis to cervical lymph node were more common than primary lymph node neoplasms. Squamous cell carcinoma constituted most of the metastasis, primary being mostly of head and neck [43] followed by lung. These go in accordance with studies done by CS Nithya [44] who concluded oropharyngeal carcinoma to be the commonest to metastasize to cervical lymph nodes, most common being ipsilateral level II lymph nodes (63.6%), followed by involvement of level I lymph nodes (51.5%), level III(10.2%), level IV (15.2%). Shah et al had similar results. [34] This is not surprising as squamous cell carcinoma of the head and neck is one of the most commonest cancers worldwide. [45] Nodal metastasis is the most important prognostic factor , especially in squamous cell carcinomas of the head and neck. It decreases the overall survival by half. [46] The level of nodal metastasis and the number and size of nodes are also significant and these factors correlate with distant metastasis. The 5 year survival of patients in studies done by Nasser et al [47] was 25%.

There was no sex predilection, as male to female ratio is almost equal to 1:1 ratio. The largest number of patients were of the age group 20-39 years, followed by 1-19 years, and most of them were diagnosed as TB lymphadenitis. Tuberculosis is a communicable disease and young individuals are exposed in the external environment as they lead a more social life. [48] Malignant metastasis to lymph node occurred at the age range

60-79 years. These findings correlated with studies done by Pandit A. at el who also reported majority of cases belonged to age group 21-40 years, followed by age group 13-20 years, most constituting of benign lesions. Malignant metastasis to lymph node also were seen mostly in the older age group population. [49]

The posterior group of cervical lymph nodes were the most frequently enlarged, constituting 71% , followed by anterior group of lymph nodes and the least affected were the supraclavicular group of lymph nodes. Patients with reactive lymphadenitis mostly presented with single discrete, firm, mobile lymph nodes following history of sore throat, or fever. TB lymphadenitis patients mostly presented as multiple matted lymph nodes, involving right side and bilaterally. Both conditions involved posterior group of lymph nodes more frequently. These findings correlate with studies done by Kheiry J at el, who also reported mostly affected lymph nodes were from the posterior triangle , followed by upper jugular and supraclavicular groups.

Tuberculous cervical enlargement is due to the infection by tubercle bacilli either in the tonsil or in lung or both. The right sided bronchus is more wider, shorter and vertical. So that, probably TB infection is also more common on the right side, like other infections, and subsequently right sided lymph nodes could have been affected more than the left side. [20]

Metastasis to lymph nodes were mostly due to squamous cell carcinoma and involved the anterior and supraclavicular group of lymph nodes, and presented as hard, fixed lymph nodes of maximum dimension of 3-4 cm. Metastatic small cell carcinoma, poorly differentiated carcinoma presented as anterior and

posterior group of lymph nodes. Metastatic adenocarcinoma presented as single hard fixed supraclavicular lymph node.

The diagnostic accuracy of FNAC in the current study had a sensitivity of 97.9 % and a specificity of 100% for TB lymphadenitis . There is 1 false negative result which failed to diagnose TB on FNAC and instead was given as reactive lymphadenitis. This could be due to failure to aspirate from the area of caseous necrosis, where a more definitive diagnosis could have been given.

The most commonest cause of granulomatous lymphadenitis in this region is tuberculosis, therefore all cases of granulomatous lymphadenitis diagnosed on FNAC, subsequently diagnosed as TB on histopatholgy were taken as true positives. Nada A. et al reported a diagnostic accuracy of 79% for tuberculous lymphadenitis, while J Rawal et al reported a sensitivity of 95.8% and a specificity of 100%, which are similar to results obtained by this study. [50]

FNAC diagnosis of metastatic squamous cell carcinoma, poorly differentiated carcinoma, adenocarcinoma, small cell carcinoma and were correlated correctly on histopathology. Therefore FNAC has been highly accurate in the diagnosis of metastatic carcinomas of the lymph node.Three cases of Non-Hodgkin's lymphoma were correctly diagnosed by FNAC. Non Hodgkin's lymphoma, Hodgkin's lymphoma can be difficult to distinguish from metastatic nasopharyngeal carcinoma [51] , however it was correctly diagnosed in this study. One case diagnosed as anaplastic large cell lymphoma by FNAC was diagnosed as undifferentiated carcinoma on histopathology. It is stated that even on

histopathology biopsy alone, these two conditions are extremely hard to differentiate [52]. The sensitivity of this one case was therefore found to be zero. These findings correlated with findings of Pandit AA et al and Nada A. et al who found that the FNAC diagnosis of metastatic carcinoma to the lymph node were accurate with histopathogy. Their study included metastatic squamous cell carcinoma, adenocarcinoma, NHL and Hodgkin's lymphoma. FNAC was seen to provide an excellent cytomorphological picture in each of these cases, giving an accuracy rate of 96%. [53]The overall sensitivity was found to be 98%, and specificity was found to be 100% in this study. These findings are similar to studies done by Nada A. at el who reported their sensitivity to be 90.5% and specificity to be 98.8%. Another study done by Sarda at el reported an accuracy rate of 97%. [54]

CONCLUSION AND RECOMMENDATION

FNA cytology appears a well established as another adjunctive method of diagnosis, since its results compare favourably in many respects with those obtained from surgical biopsy. This fact is illustrated by the high sensitivity and specificity encountered in this study and others. In malignant lymphadenopathies, this inexpensive, relatively painless and rapid technique may not only help in the primary diagnosis of tumors, but remains a useful method of following up patients with known malignancies and even in guiding therapy.

Fine needle aspiration cytology is found to be a rapid and prompt way of finding out metastasis to the cervical lymph node and hence providing rapid treatment to the patient, therefore giving a good prognosis to the patient.

In this study a total of 101 cases were included in which excisional biopsy was done following fine needle aspiration cytology. Majority of cases included benign lesions (83%) followed by malignant conditions (17%). Reactive lymphadenitis constituted the majority of benign conditions (44%), followed by tuberculous lymphadenitis(37%). Squamous cell carcinoma from the head and neck region constituted the majority of metastasis to the cervical lymph nodes.

Fine needle aspiration cytology had a sensitivity of 98% and a specificity of 100%. Positive predictive value was found to be 97.9% and negative predictive value 100%.

Therefore FNAC can be used as a very reliable , accurate, cost effective , precise and friendly diagnostic procedure for determining diagnosis of cervical lymphadenopathies.

Recommendation

This easy, effective and patient friendly procedure can be a useful tool in not only determining the causes of cervical lymphadenopathy, but the prognosis of a malignant disease can take a toll by this simple procedure. Since it gives a high accuracy rate, it can be used a reliable procedure.

But however in doubtful cases, correlation with histopathological examination is recommended.

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PROFORMA

Name: Case No:

Address:

Age:

Sex:

Clinical Details of lump:

Onset:

Site

Duration:

Associated pain:

Associated fever/ weight loss/night sweats etc:

Family history of TB/malignancy:

Relevant past history:

Clinical findings:

Site: right [ ] left [ ] bilateral [ ]

Anterior cervical [ ] Poterior cervical [ ] supraclavicular [ ]

Single [ ] Multiple [ ]

Size: <1 cm [ ] 1-2 cm [ ] 3-4cm [ ]

Consistency: Firm [ ] Hard [ ] Rubbery [ ] Matted [ ]

Mobile [ ] Fixed [ ]

Overlying skin:

Any other relevant findings:

Investigations:

CBC:

Mantoux test (if available):

Radiological findings (if available):

The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy

THESIS

SUBMITTED TO THE TRIBHUVAN UNIVERSITY
IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE
DEGREE OF DOCTOR OF MEDICINE
IN PATHOLOGY

BY
Dr. Shimal Thasneem

Kathmandu, Nepal, 2007

DECLARATION

I hereby declare that this thesis work on "The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy" has not been submitted in candidature for any degree to any university. My permission for availability of this thesis (as part or whole) for photocopied or used for other research purposes.

Dr Shimal Thasneem
September 2007

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The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy

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A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Medicine in Pathology of the Tribhuvan University, Nepal

Dr. Shimal Thasneem

Based on the studies conducted at the Department of Pathology,
Tribhuvan University Teaching Hospital,
Kathmandu, Nepal.

Guide: Prof Gita Sayami
Department of Pathology,
T.U. Teaching Hospital

CERTIFICATE

This is to certify that the work contained in the thesis entitled **The role of fine needle aspiration cytology in determining the causes of cervical lymphadenopathy** is the result of the original investigative study undertaken by Dr Shimal Thasneem in the Department of Pathology under our direct supervision and guidance.

Prof. Gita Sayami MD, PhD.
Guide, Head of Dept and Professor,
Department of Pathology,
TU Teaching Hospital.

Dr.R.C. Adhikari, MBBS, MD
Co-guide, Assistant Professor,
Department of Pathology,
TU Teaching Hospital

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Dr Shimal Thasneem
September 2007

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Shimal Thasneem.

Dedicated to my family

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LIST OF ABBREVIATIONS

TB LN	-	Tuberculous lymphadenitis
Reac LN	-	Reactive lymphadenitis
SCC	-	Squamous cell carcinoma
SmCC	-	Small cell carcinoma
PDC	-	Poorly differentiated carcinoma
Adenoca	-	Adenocarcinoma
NHL	-	Non-Hodgkin's lymphoma
HL	-	Hodgkin's lymphoma
Undiff ca	-	Undifferentiated carcinoma
FNAC	-	Fine needle aspiration cytology
HPE	-	Histopathological examination
TUTH	-	Tribhuvan University Teaching Hospital

Abstract

Introduction:

Lymphadenopathy is one of the commonest clinical presentations of patients attending the out patient department. The role of fine needle aspiration cytology in diagnosing lymphadenopathy has become widely accepted as a reliable, cost effective procedure that has several advantages over excisional biopsy.

Objectives:

The main objective of this study was to analyze the causes of cervical lymphadenopathy and to determine the role of fine needle aspiration cytology in diagnosing cervical lymphadenopathy.

Results:

A total of 299 cases of cervical lymphadenopathy presented for FNAC from November 2005- November 2006 to Department of Pathology, TUTH. Of which subsequent biopsy were available in 101 cases. The histopathological diagnosis of these 101 cases were compared with the FNAC diagnosis, taking biopsy as the gold standard.

Benign lesions constituted majority of conditions to present with enlarged cervical lymph nodes, comprising of 83%, and malignant metastasis constituting 17%. Of the benign lesions reactive lymphadenitis was the most prevalent (44%), followed by tuberculous lymphadenitis (37%). Squamous cell carcinoma (6%) was found to be the most common metastasis to cervical lymph node, mostly to upper

anterior group of cervical lymph nodes (5%). Posterior cervical lymph nodes were the most frequent lymph node groups to be involved (71%), followed by anterior cervical group (28%).

Senstivity and specificity of FNAC were found to be 98% and 100% respectively. For benign lesions, sensitivity and specificity were 98.8% and 100%, and for malignant lesions it was found to be 94.4% and 100%. The positive predictive value was 100% and negative predictive value was 99.7%. These findings were in accordance with several studies done previously.

Conclusion:

Therefore FNAC was found to be a useful, reliable method with high accuracy rate in determining the causes of cervical lymphadenopathy.

INTRODUCTION

INTRODUCTION

FNAC has become an integral part of the initial diagnosis and management of patients presenting with lymphadenopathy. This simple technique has recently gained wide acceptance, since it offers a high degree of accuracy, lending itself to outpatient diagnosis and thus making savings in the cost of hospitalization. It has several advantages over excisional biopsy. The procedure requires minimal time, whereas on the other hand excisional biopsy often requires time away from work, preoperative investigations, exposure to risk of anesthesia and postoperative infections. [1]

FNAC is an easy and cost effective procedure which is patient friendly and a quick result can be obtained thereby enabling the surgeon to start treatment early, whereas biopsy is time taking, more painful causing unwarranted bleeding at times and delays the treatment because it needs more time for processing and hence reporting. In the developing third world countries where a blade carries a surgical impression and a needle enjoys a therapeutic image, the potential role of FNAC is far reaching.

Lympahadenopathy is one of the commonest clinical presentations of patients attending the outpatient department. Lymphadenopathy refers to nodes that are abnormal in either size, consistency or number. There are various classifications of lymphadenopathy , but a simple system is to classify lymphadenopathy as " generalized ", if lymph nodes are enlarged in two or more

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Lympahadenopathy is one of the commonest clinical presentations of patients attending the outpatient department. Lymphadenopathy refers to nodes that are abnormal in either size, consistency or number. There are various classifications of lymphadenopathy , but a simple system is to classify lymphadenopathy as " generalized ", if lymph nodes are enlarged in two or more

non-contiguous areas or "localized" if only one area is involved. Approximately about three fourths of patients present with localized lymphadenopathy and about one fourth of patients present with generalized lymphadenopathy in a primary care setting. [2, 3 4] Cervical lymphadenopathy can result from a vast array of disease processes, representing infections, malignancies, autoimmune diseases, iatrogenic causes etc.

As cervical lymphadenopathy can present in diseases of variety of causes, the use of fine needle aspiration cytology in diagnosis of the causes of cervical lymphadenopathy has become an easy and effective method. More to it, the prognosis of a particular disease takes its toll by the use of this effective method.

In this study the diagnostic role of fine needle aspiration cytology and excision biopsy was compared, and the frequency of diseases causing cervical lymphadenopathy was evaluated.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

GENERAL-To analyse the causes of cervical lymphadenopathy.

SPECIFIC:

1. To determine the frequency of neoplastic and non-neoplastic diseases causing cervical lymphadenopathy.

2. To find out age and sex distribution of patients with cervical lymphadenopathy

3. To determine the sensitivity and specificity of FNAC in diagnosing the diseases causing cervical lymphadenopathy.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design- prospective

Study period- 1 year

Place- Department of Pathology , TUTH, Katmandu, Nepal

Sampling size- 100 cases of fine needle aspirated cases and subsequent excisional biopsy of the same lymph node.

INCLUSION CRITERIA

All excised lymph node biopsy specimens with fine needle aspirated lymph nodes, irrespective of age and sex, were included in this study.

EXCLUSION CRITERIA

Patients without consent.

Inadequate aspirates that were not available for repeat aspirations were excluded from the study.

PROCEDURE

The skin above the area to be aspirated was cleared with an antiseptic solution. After locating the mass a fine needle of 23 guage was passed through the mass. The needle was inserted and withdrawn several times, and the material aspirated by pulling the plunger of the syringe. After the needle was withdrawn the aspirate was blown onto the slide, and smears made. Two slides were immediately kept in propanolol for Papanicolaou stain and two slides were air dried for Giemsa stain. [5]

Papanicolaou method of staining

Smears were put in 95% alcohol

After fixation, slides were transferred without drying directly from alcohol to 90% alcohol, 80% alcohol , 70% alcohol and water to distilled water.

Stained in Harris haematoxylin (modified) for 10 minutes.

Rinsed in water to prevent cells from being washed off.

Differentiate carefully the nuclear staining in 1% hydrochloric acid and in 70% alcohol.

Placed gently in water for five minutes to wash out acid thoroughly and blue the nuclei.

Rinsed in distilled water and transfer through 70% alcohol.

Stained in OG 6 for 6-10 minutes.

Washed with 70% alcohol

Stained with EA 36 for 5 minutes.

Washed in 90%, 100% alcohols.

Put in xylene I and II

Mounted in DPX.

Giemsa Staining

Air dried smears were fixed in a jar of methanol for 20-30 minutes.

Stained with Giemsa stain diluted with nine parts of phosphate buffer for 20-30 minutes.

Washed with distilled water

Dried in air

Mounted with DPX.[6]

Specimen collection for histopathology

The patients were then subjected to lymph node excision biopsies. Patients underwent surgery at a later date and the surgical specimen subjected to histopathological examination.

The specimens were processed by the usual graded alcohol dehydration in the automated histokinette. An overnight schedule of 16-18 hours were used. The tissues were the embedded in paraffin wax and sliding microtome sectioning was done with a thickness of 3-4 microns. These sections were fixed in glass slides, dewaxed and made ready for staining with haematoxylin and eosin stains.

Haematoxylin and eosin staining

Dewaxed in xylene

Treatment through graded alcohol of decreasing concentration i.e. 100%, 90%, 80%, 70% to water.

Stained with Harris haematoxylin for 15 minutes.

Washed in water for five minutes.

Treatment in 1% acid alcohol (1% HCL in 70% alcohol) for 5-10 seconds.

Washed in water for 5 minutes, treatment with lithium carbonate for 1 minute.

Washed in water.

Stained with 0.5% eosin for 10 minutes.

Treatment through graded alcohol of increasing concentration i.e. 70%, 80%, 90%.

Treatment with xylene for clearance.

Mounted with DPX. [6]

LITERATURE REVIEW

Literature review

Anatomical considerations

The neck lymph nodes are divided into five major groups.

Significant Nodal Groups in the neck

Deep lateral cervical.

Submental-submandibular.

Parotid.

Retropharyngeal.

Anterior cervical.

Deep Lateral Cervical Group

A. Internal jugular chain (deep cervical).

B. Spinal accessory chain (posterior triangle).

C. Transverse cervical (supraclavicular).

The highest jugular digastric node near the angle of the mandible is called the "sentinel" node.

The "signal" node is the lowest along the internal jugular chain called the virchow nodes.

If only a virchow node is present, then one should check the abdomen and/or chest for primary source of metastasis.

The internal jugular chain is divided into:

High: Above the hyoid.

Mid: Between hyoid and cricoid.

Low: Below the cricoid.

The internal jugular chain is a common final pathway that receives drainages from parotid, retropharyngeal, and submandibular/submental groups. Drainage from the internal jugular chain is into the subclavian vein and/or internal jugular vein and/or into the right lymphatic duct and thoracic duct.

Spinal accessory (posterior triangle) nodal group receives occipital/mastoid, lateral neck, scalp, nasopharyngeal sources. Abnormal spinal accessory nodes may indicate the presence of an early nasopharyngeal cancer.

Transverse cervical chain receives drainage from deep cervical, supraclavicular, subclavicular, upper chest, anterior lateral neck.

Sources: The drainage is the same as for the internal jugular chain.

Submental/Submandibular Chain

Submental nodes receive drainage from adjacent skin, lips, floor of the mouth, and drain to the submandibular nodal group. Submandibular nodes are extra glandular and receive drainage from anterior face, floor of the mouth, anterior oral cavity, and submental nodal group. Drainage is to the high internal jugular chain.

Parotid Nodal Group

Intra or extra glandular nodes.

Receives drainage from external auditory canal, eustachian tube, adjacent skin, buccal mucosa (squamous cell carcinoma and melanoma of skin frequently metastasize to this group). Drainage is to high internal jugular chain.

Retropharyngeal Nodal Group

Two compartments: Medial and lateral retropharyngeal.

Medial retropharyngeal receives drainage from nasopharynx and oropharynx and drains to high internal jugular chain.

Lateral retropharyngeal (nodes of Rouvierre) are located just medial to the internal carotid artery. Drainage is the same as for the medial retropharyngeal nodes.

Early sign of nasopharyngeal cancer may be the presence of abnormal lateral retropharyngeal node in the patient over forty years.

Anterior Cervical Nodal Group

Anterior jugular: superficial. Follows the course of the external jugular vein. Receives drainage from skin and muscles of the anterior neck. Drains to the thoracic duct.

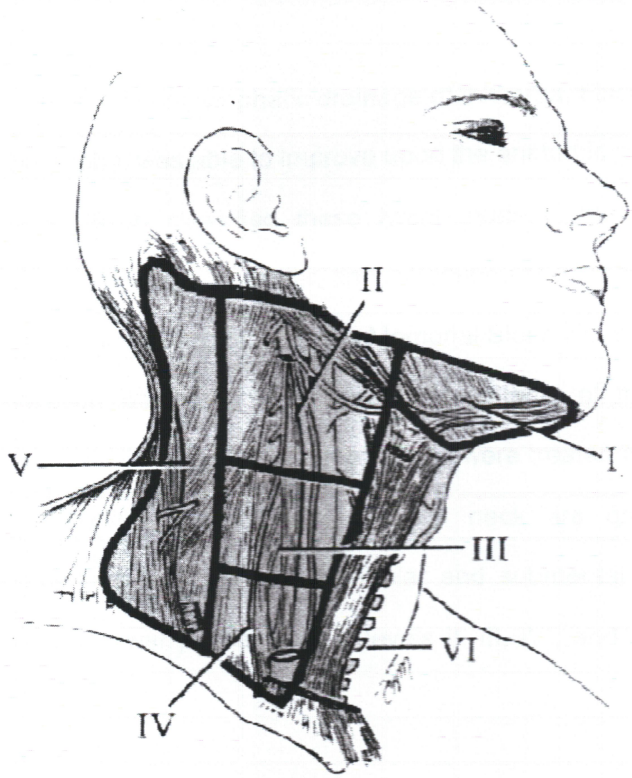
Paraesophageal group: Tracheal esophageal groove nodes and delphian node. Abnormal delphian node is often an indicator of subglottic laryngeal cancer

extension.

This group receives drainages from hypopharynx, larynx, thyroid, and esophagus. Drainage is then to the thoracic duct. [7]

Classification to describe the patterns of metastasis

The lymph nodes of the neck can be divided into six levels within the defined anatomic triangles. These groups and the areas that they drain are particularly important when locating and working up a "neck mass" or possible malignancy. The groups and drainage areas are as follows:



- **I--Submental and submandibular nodes**
- **II--Upper jugulodigastric group**

- **III--Middle jugular nodes** draining the naso- and oropharynx, oral cavity, hypopharynx, larynx.
- **IV--Inferior jugular nodes** draining the hypopharynx, subglottic larynx, thyroid, and esophagus.
- **V-- Posterior triangle group**
- **VI--Anterior compartment group** [8]

In his 1964 study of lymphatic drainage of this area, Fisch, using the technique of lymphography, was able to improve upon the anatomic classification proposed by Rouviere. Fisch classified these lymph nodes into 5 categories: junctional, jugular, spinal, supraclavicular, and retroauricular. However, the nomenclature in popular use today comes from the Memorial Sloan Kettering Cancer Center. This classification was used to describe the patterns of metastatic dissemination observed in more than 1000 patients who were treated at the center with radical neck dissection. Lymph nodes in the neck are grouped into levels I-V, corresponding with the submandibular and submental nodes (level I); upper, middle, and lower jugular nodes (levels II, III, IV); and posterior triangle nodes (level V).

Submental/ submandibular nodes (Level I)

These are bound by the body of the mandible superiorly, stylohyoid muscle posteriorly, and the anterior belly of the digastric muscle on the contralateral side

anteriorly. This level may be divided into level Ia, which refers to the nodes in the submental triangle (bound by the anterior bellies of the digastric muscles and the hyoid bone), and Ib, which refers to the submandibular triangle nodes. The nodes of level Ia are at greatest risk of harboring metastasis from cancers that arise from the floor of mouth, anterior tongue, anterior mandibular alveolar ridge, and lower lip, while the nodes of level Ib often receive metastasis from cancers of the oral cavity, anterior nasal cavity, soft tissue structures of the mid face, and submandibular gland.

Closely related, although not strictly a part of the level I group of nodes, are the perifacial nodes, related to the facial vessels above the mandibular margin, and the buccinator nodes, which may become involved with metastasis from tumors in the buccal mucosa, nose, and soft tissues of the cheek and lips.

Upper jugulodigastric group (Level II)

These are related to the upper third of the jugular vein, extending from the skull base to the inferior border of the hyoid bone. The anterior border of level II is the stylohyoid muscle, and the posterior border is the posterior border of the sternocleidomastoid muscle. The spinal accessory nerve, which travels obliquely across this area, is used as a landmark to subdivide this group into IIb, the portion above and behind the nerve, and IIa, the part that lies anteroinferiorly and closer to the internal jugular vein.

The nodes in level II are at greatest risk of harboring metastasis from cancers that arise from the oral cavity, nasal cavity, nasopharynx, oropharynx, hypopharynx, larynx, and parotid gland.

Middle jugular nodes (Level III) nodes

These are located between the hyoid superiorly and a horizontal plane defined by the inferior border of the cricoid cartilage. The sternothyroid muscle marks the anterior limit of level III, and the posterior border of the sternocleidomastoid muscle is the posterior border. Level III most commonly receives metastasis from cancers that originate in the oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx.

Inferior jugular nodes (Level IV)

These nodes refer to the group of nodes related to the lower third of the jugular vein. These nodes are located between the inferior border of the cricoid cartilage and the clavicle, and, like level III, the anterior boundary is the sternothyroid muscle, and the posterior border is the posterior border of the sternocleidomastoid muscle. The nodes of level IV commonly harbor metastasis from cancer that originates in the larynx, hypopharynx, thyroid, and cervical esophagus.

Posterior triangle group (Level V)

These nodes refer to the lymph nodes located in the posterior triangle of the neck. These include the spinal accessory, transverse cervical, and supraclavicular group of nodes. Level V is bound anteriorly by the posterior border of the sternocleidomastoid muscle and posteriorly by the anterior border of the trapezius muscle. Level V extends from the apex of the convergence of the sternocleidomastoid and trapezius muscle superiorly to the clavicle inferiorly. This level is subdivided by a plane defined by the inferior border of the cricoid cartilage into level Va superiorly and level Vb inferiorly. Level Va contains the nodes associated with the spinal accessory nerve, and level Vb contains the transverse cervical and supraclavicular nodes. The posterior triangle nodes are at greatest risk for harboring metastasis from cancers that arise in the nasopharynx, oropharynx, and skin of the posterior scalp and neck. The anterior, or central, compartment of the neck, located between the carotid arteries of the 2 sides, is rich in lymphatics that drain the thyroid gland, subglottic larynx, cervical trachea, hypopharynx, and cervical esophagus. Lymph nodes in this compartment are located in the tracheoesophageal groove (paratracheal nodes), in front of the trachea (pretracheal nodes), around the thyroid gland (perithyroidal nodes), and on the cricothyroid membrane (precricoid or Delphian node). Lymph nodes in the central compartment are not routinely excised in radical neck dissection; most commonly, they are removed during surgery for thyroid, laryngeal, and hypopharyngeal cancer. This group of nodes, although not

included in the original Memorial Sloan Kettering classification, is referred to as level VI. [9]

Probable Source of Nodal Metastasis

Submandibular/submental nodes: Oral cavity, submandibular gland.

Upper jugulodigastric nodes: Nasopharynx, oropharynx, parotid, supraglottic larynx.

Middle jugular nodes: Oropharynx, hypopharynx, supraglottic larynx.

Inferior jugular nodes: Subglottic larynx, hypopharynx, esophagus, thyroid.

Posterior triangle nodes: Nasopharynx, oropharynx.

Anterior compartment: Thyroid, larynx, lung.

Bilateral nodes are common with cancers of soft palate, tongue, epiglottis, and nasopharynx.

Pathological considerations

The approximately 600 lymph nodes in the body are strategically located along the course of lymphatics, which permits them to filter lymphatic fluid and encounter potential pathogens. The lymph nodes are populated predominantly by macrophages, dendritic cells, B lymphocytes , and T lymphocytes, which function together as a part of the normal immune response to microorganisms and foreign proteins. Swelling of lymph nodes induced by lymphocyte proliferation is a

normal response to antigen stimulation . Because children and adolescents are frequently exposed to new antigens, they commonly have enlarged nodes. Soft, flat nodes (<1 cm in diameter) often are palpable in the neck and axilla of healthy individuals , especially in children , and inguinal nodes upto 1 to 2 cm are generally normal in adults.The term lymphadenopathy refers to nodes that are abnormal in size, character (consistency), or number. Lymphadenopathy is "generalized" if nodes in two or more noncontiguous areas are involved and "localized" if just one area (or two contiguous areas) is involved. Generalized lymphadenopathy usually indicates systemic disease. In the primary care setting about 75% of patients with enlarged nodes present with localized lymphadenopathy. Lymph nodes themselves are seldom the primary site of a bacterial infection, but swollen nodes typically are present in an area that receives drainage from an infected site. [4]Lymph nodes, in conjunction with the spleen, tonsils, adenoids, and Peyer patches, are highly organized centers of immune cells that filter antigen from the extracellular fluid. Directly interior to the fibrous capsule is the subcapsular sinus. This allows lymph, an ultrafiltrate of blood, to traverse from the afferent lymph vessels, through the sinuses, and out the efferent vessels. In addition to supplying lymph with a channel for lymph flow, the sinuses are studded with macrophages, which remove 99% of all delivered antigens. Interior to the subcapsular sinus is the cortex containing primary follicles, secondary follicles, and the interfollicular zone. Follicles within the cortex are major sites of B-cell proliferation, whereas the interfollicular zone is the site of antigen-dependent T-cell differentiation and proliferation. The deepest structure

within the lymph node is the medulla, consisting of cords of plasma cells and small B lymphocytes that are architecturally arranged near the sinuses to facilitate immunoglobulin secretion into the exiting lymph. The lymph node, with its high concentration of lymphocytes and antigen-presenting cells, is an ideal organ for the delivery of antigen that gains access through the skin or gastrointestinal tract. Nodes have considerable capacity for growth and change. Lymph node size depends on the person's age, the location of the lymph node in the body, and antecedent immunological events. In neonates, lymph nodes are barely perceptible. Thereafter begins a progressive increase in total lymph node mass until later childhood. Lymph node atrophy begins during adolescence and continues throughout life.

Pathophysiology:

Most lymphadenopathy in children is due to benign self-limited disease because self-limited viral or bacterial infections are the most common causes. Lymphadenopathy can be caused by an increase in normal lymphocytes and macrophages during a response to an antigen (eg, viral illness), nodal infiltration by inflammatory cells in response to an infection in the nodes themselves (lymphadenitis), proliferation of neoplastic lymphocytes or macrophages (lymphoma), or infiltration of nodes by metabolite-laden macrophages in storage diseases (Gaucher disease).

Frequency:

The precise incidence of lymphadenopathy is not known. Lymphadenopathy is one of the most common clinical problems encountered in pediatrics. It is often difficult to determine whether adenopathy is simply a normal response to frequent viral infections within an age group or if it is significant enough to consider more serious underlying disease. In Asia, common viral and bacterial infections are overwhelmingly the most common cause of adenopathy. Infectious mononucleosis and cytomegalovirus (CMV) are important etiologies, but adenopathy is usually caused by common viral upper respiratory tract infections. Localized lymphadenitis is most often caused by staphylococci and beta-hemolytic streptococci. Other infections, such as HIV, malignancies, and autoimmune diseases, are less common causes of adenopathy in Asia. Infections that are commonly observed in Asia and the developing countries are less commonly observed in United States. These include tuberculosis, typhoid fever, leishmaniasis, trypanosomiasis, schistosomiasis, filariasis, and fungal infections. HIV infections must be considered strongly in areas of high incidence in the United States.

Mortality/Morbidity:

Mortality and serious morbidity caused by adenopathy are unusual given the common infectious etiologies. HIV is an uncommon cause of adenopathy, but its associated mortality requires consideration. Malignancies, such as squamous

cell carcinomas, adenocarcinomas, leukemia, and lymphomas, are the primary causes of mortality. Significant morbidity and mortality are also associated with rare serious infections, autoimmune disorders (eg, juvenile rheumatoid arthritis, systemic lupus erythematosus), histiocytoses, and storage diseases.

Race:

Race is not a major factor in most disorders associated with lymphadenopathy.

Sex:

Sex is not a major factor associated with lymphadenopathy.

Age:

Adenopathy is most common in young children whose immune systems are responding more frequently to newly encountered infections. Adenopathy is uncommon in the neonate who usually has not had significant exposure to infectious etiologies and in whom other disorders associated with lymphadenopathy are rare. The peak prevalence of leukemia is in children younger than 10 years, whereas Hodgkin disease is observed more often in adolescents. [10]

Cervical Lymphadenopathy

Cervical nodes drain the tongue, external ear, parotid gland, and deeper structures of the neck, including the larynx, thyroid, and trachea. Inflammation or direct infection of these areas causes subsequent engorgement and hyperplasia of their respective node groups. Adenopathy is most common in cervical nodes in children and usually is related to infectious etiologies. Lymphadenopathy posterior to the sternocleidomastoid typically is a more ominous finding, with a higher risk of serious underlying disease.

Infectious causes

Cervical adenopathy is a common feature of many viral infections. Infectious mononucleosis often manifests with posterior and anterior cervical adenopathy. Firm tender nodes that are not warm or erythematous characterize this lymph node enlargement. Other viral causes of cervical lymphadenopathy include adenovirus, herpesvirus, coxsackievirus, and CMV. In herpes gingivostomatitis, impressive submandibular and submental adenopathy reflects the amount of oral involvement. Bacterial infections cause cervical adenopathy by causing the draining nodes to respond to local infection or by the infection localizing within the node itself as a lymphadenitis. Bacterial infection often results in enlarged lymph nodes that are warm, erythematous, and tender. Localized cervical lymphadenitis typically begins as enlarged, tender, and then fluctuant nodes. The

appropriate management of a suppurative lymph node includes both antibiotics and incision and drainage. Antibiotic therapy should always include coverage for Staphylococcus aureus and Streptococcus pyogenes. In patients with cervical adenopathy, any history of recent or ongoing sore throat or ear pain and examination of the oropharynx, paying special attention to the posterior pharynx and the dentition are important . The classic manifestation of Group A streptococcal pharyngitis is sore throat, fever, and anterior cervical lymphadenopathy. Other streptococcal infections causing cervical adenopathy include otitis media, impetigo, and cellulitis. Atypical mycobacteria cause subacute cervical lymphadenitis with nodes that are large and indurated but not tender. The only definitive cure is removal of the infected node. Mycobacterium tuberculosis may manifest with a suppurative lymph node identical to that of atypical mycobacterium. Intradermal skin testing may be equivocal. Catscratch disease, caused by *Bartonella henselae,* presents with subacute lymphadenopathy often in the cervical region. The disease develops after the infected pet (most likely a kitten) inoculates the host, usually through a scratch. Approximately 30 days later, fever, headache, and malaise develop, along with adenopathy that often is tender. Several lymph node chains may be involved. Suppurative adenopathy occurs in 10-35% of patients. Antibiotic therapy has not been shown to shorten the course.

Malignant metastasis to cervical lymph nodes

Cancers of the oropharynx, squamous cell carcinoma accounts for the most frequent metastasis to cervical lymph nodes, mostly occupying the submandibular/submental nodes and upper jugulodigastric lymph nodes.[11] Other studies done by W. Giridharan et al also favours this finding as they report most common tumor to metastasize to cervical lymph nodes were squamous cell carcinoma (73%) , followed by lymphomas (28%) and adenocarcinoma (27%). [12] Mostafa et al [13] also reports squamous cell carcinoma to be the most frequent metastasis to cervical lymph node. This is not surprising as more than 90% of head and neck tumors comprise of squamous cell carcinoma.[14] Studies done by Nada A Alwan [15] and Bezabiah [16] report that lymphomas constituted the main pathology in malignant involvement (26%), while metastatic lesions formed 16.7% and leukemias 2%.

Noninfectious and infectious etiologies in children

Malignant childhood tumors develop in the head and neck region in 27% of cases. In the first 6 years of life, neuroblastoma, leukemia, non-Hodgkin lymphoma, and rhabdomyosarcoma (in order of decreasing frequency) are most common in the head and neck region. In children older than 6 years, Hodgkin disease and non-Hodgkin lymphoma both predominate. Children with Hodgkin disease present with cervical adenopathy in 80-90% of cases as opposed to 40% of those with non-Hodgkin lymphoma.

Kawasaki disease is an important cause of cervical adenopathy. These children have fever for at least 5 days, and cervical lymphadenopathy is one of the 5 diagnostic criteria (of which 4 are necessary establish the diagnosis). Submaxillary and submental lymphadenopathy: These nodes drain the teeth, tongue, gums, and buccal mucosa. Their enlargement usually is the result of localized infection, such as pharyngitis, herpetic gingivostomatitis, and dental abscess.

Occipital lymphadenopathy:

Occipital nodes drain the posterior scalp. These nodes are palpable in 5% of healthy children. Common etiologies of occipital lymphadenopathy include tinea capitis, seborrheic dermatitis, insect bites, orbital cellulitis, and pediculosis. Viral etiologies include rubella and roseola infantum. Uncommonly, occipital lymphadenopathy may be noted after enucleation of the eye for retinoblastoma.

Preauricular lymphadenopathy:

Preauricular nodes drain the conjunctivae, skin of the cheek, eyelids, and temporal region of the scalp and rarely are palpable in healthy children. The oculoglandular syndrome consists of severe conjunctivitis, corneal ulceration, eyelid edema, and ipsilateral preauricular lymphadenopathy. Chlamydia trachomatis and adenovirus can cause this syndrome.

Supraclavicular lymphadenopathy

Supraclavicular nodes drain the head, neck, arms, superficial thorax, lungs, mediastinum, and abdomen. Left supraclavicular nodes also reflect intra-abdominal drainage and enlarge in response to malignancies in that region. This is particularly true when adenopathy in this region occurs in the absence of other cervical adenopathy.

Right supraclavicular nodes drain the lung and mediastinum and are typically enlarged with intrathoracic lesions.

Serious underlying disease is frequent in children with supraclavicular adenopathy and always merits further evaluation. The potential for malignancy necessitates peripheral blood counts, skin testing for tuberculosis, and chemical studies, including uric acid, lactate dehydrogenase, calcium (Ca), phosphorus (P), and renal and hepatic function studies. Chest radiography and possibly computerized tomography are indicated. Several important infections may occur with supraclavicular adenopathy,including tuberculosis, histoplasmosis, and coccidioidomycosis. Early lymph node biopsy should be considered in children with supraclavicular adenopathy.[10]

Prognosis according to level of lymph node metastasis

Studies done by Jones AS et al reports that 5 year survival of metastatic squamous cell carcinoma to the cervical lymph nodes were 51% and survival fell

from increasing to decreasing node level (submandibular/submental to posterior cervical group), being 37% for submandibular lymph nodes , 32% for deep cervical lymph nodes , and 25% for lower deep cervical lymph nodes. The 18 month survival for supraclavicular and posterior triangle nodes were 21%. Multivariate analysis confirmed that as the level of the nodes fell from submandibular region to supraclavicular region the prognosis worsened. Upper jugulodigastric cervical lymph nodes were most commonly involved with regards to all primary sites and found in 69% of all neck node metastasis. [17]

Ipsilateral metastasis to cervical lymph nodes were seen as the common presentation to submandibular/submental nodes and upper jugulodigastric lymph nodes, and are not associated with prognosis of the patient.[18,19]

Literature of Fine needle aspiration cytology

FNA for cytologic evaluation of a neck mass was first reported by Kun in 1847. However, the procedure did not gain wide acceptance in medicine at that time. In the 1930s, Memorial Sloan Kettering rediscovered the utility of needle biopsy of head and neck masses. The use of large-bore needles at that time led to frequent complications, 1 of which was occasional seeding of the tumor along the biopsy tract. The frequent morbidity associated with this procedure preventedwidespread acceptance of this technique in other centers of America. A resurgence of FNA occurred in the 1950s, led by physicians in Sweden. FNA was commonly used for cytologic examination of metastatic lesions in the neck with excellent results. Since then, FNA of solitary neck masses has become a

well-accepted, safe, and cost-effective procedure in the diagnosis of neck masses.[20] Countries with the most developed aspiration biopsy are Sweden, Slovenia and India. At Karolinska hospital (Stockholm, Sweden), the annual volume average seven thousand aspirates; at Institute of Oncology (Ljubljana, Slovenia) ten thousand.[21] FNA is a simple office procedure requiring a few minutes to complete. If cytotechnologists and pathologists are available, diagnosis can often be made immediately.

FNA has several advantages over excisional biopsy. In today's economic environment, cost savings is an important consideration in medicine. FNA is also more convenient for patients and their families. The procedure requires only an office visit with minimal loss of time from work. On the other hand, excisional biopsy often requires time off from work, preoperative blood tests, and often, radiographic and cardiac testing. Furthermore, surgery exposes patients to the risks of anesthesia, postoperative infection, and the possibility of tumor seeding. A percentage of patients may require overnight admission to the hospital and extra time from work. However FNA for cervical lymph nodes has several limitations. Failure to establish an accurate diagnosis may be because of sampling error. In these circumstances, repeat aspiration is suggested, and excisional biopsy may be considered. Personnel responsible for handling, processing (experienced cytotechnologist), and reading (cytopathologist) of FNA samples must be well trained. Interobserver variability must be minimized.

No medical procedure is without risks. Due to the small size of the needle, the chance of spreading a cancer or finding cancer in the needle path is very small. Other complications are rare; the most common is bleeding. If bleeding occurs at all, it is generally seen as a small bruise. Patients who take aspirin, or blood thinners, are more at risk to bleed. However, the risk is minimal. Infection is rarely seen.[22]

Fine needle aspiration cytology in cervical lymphadenopathy

Fine needle aspiration cytology in the diagnosis of cervical lymphadenopathy is found to be an inexpensive, useful tool with high diagnostic accuracy. Mondal A et al found a diagnostic accuracy of 100% for benign conditions of the lymph nodes like tuberculous lymphadenitis [23] and pyogenic lymphadenitis, giving an overall accuracy of 96.2%. [24] Similar observations were made by Prasad et al having an overall accuracy of 91.5%. [25] Similarly malignant metastasis to the cervical lymph node had a high diagnostic accuracy as given by Shaha et al [26] and LeeJY [27] et al, who reported 96% and 95.7% respectively. Accuracy for malignant tumors with correct diagnosis being made in case of metastatic squamous cell carcinomas, adenocarcinomas, lymphomas and thyroid malignancies. Lymphomas have a sensitivity of 82.5%, and benign conditions have a sensitivity of 97.3%. Gupta et al [28] reports metastatic carcinoma to have a higher diagnostic value , however diagnosis of reactive hyperplasia and Non

Hodgkin's lymphoma could be problematic. Metastatic thyroid malignancies have an accuracy rate of 79.1%. [29] Of these papillary carcinomas constituted the majority of conditions. [30] Most of the thyroid malignancies like papillary carcinoma, Hurthle cell carcinoma, Anaplastic carcinoma did not produce much discrepancies in obtaining the accurate diagnosis. To obtain a diagnosis of metastatic small cell carcinoma and Non Hodgkins Lymphoma could be challenging. Studies conducted by De Las et al [31] found out the presence of evenly dispersed fine granular chromatin, paranclear blue inclusions and nuclear fragments were statistically significant in differentiating small cell carcinoma from Non-Hodgkin's lymphoma. Diagnostic discrepancies can occur when differentiating anaplastic large cell lymphoma, undifferentiated carcinoma and some cases of Hodgkin's lymphoma.[32]Immunophenotyping can be of value in these instances. Supraclavicular lymph nodes were most likely to be involved by malignant metastasis. Malignancy was present in 55% of the supraclavicular lymph nodes by studies done by Ellison et al [33] and 85% by Steel et al [34], and their primary being mostly from lungs, breast and cervix. Sensitivity of fine needle aspiration was seen to be 97% and specificity 98%. FNAC in children and adolescents were compared in a study done by Ponder et al [35] who obtained FNAC samples from children <10 years and adolescents 4.7% of inconclusive results were reported in the younger age group, and few inconclusive results in the older age group. Majority of conditions included benign reactive conditions than malignant tumors and FNAC was found to be a reliable tool in diagnosing cervical lymphadenopathy in children. FNAC in patients with acquired

immunodeficiency syndrome [36] with cervical lymphadenopathy and homosexuals [37] were found to give prompt diagnosis and rapid initiation of treatment which led to symptomatic improvement. Of the conditions that affect the cervical lymph node, tuberculous lymphadenitis were found to be more prevalent in low socioeconomic groups, such as parts of India. [38] However two studies done in Middle east [39, 40], such as Kingdom of Saudi Arabia shows Tuberculous lymphadenitis as more prevalent. FNAC showed a sensitivity of 76.9% in study done by Hsu C et al. [41]FNAC is therefore reliable, cheap, cost-effective as well as rapid and is followed by fewer complications as compared to excision biopsy.

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RESULT

Results:

A total of 1859 fine needle aspirations were done in the Dept of Pathology during Nov 2005 to Nov 2006. Among them, 299 cases were from cervical lymph nodes. Subsequent biopsy following FNAC were done in 101 cases, the remaining 198 cases biopsy were not available.

Figure : 1: Total results of FNAC in 1 year period

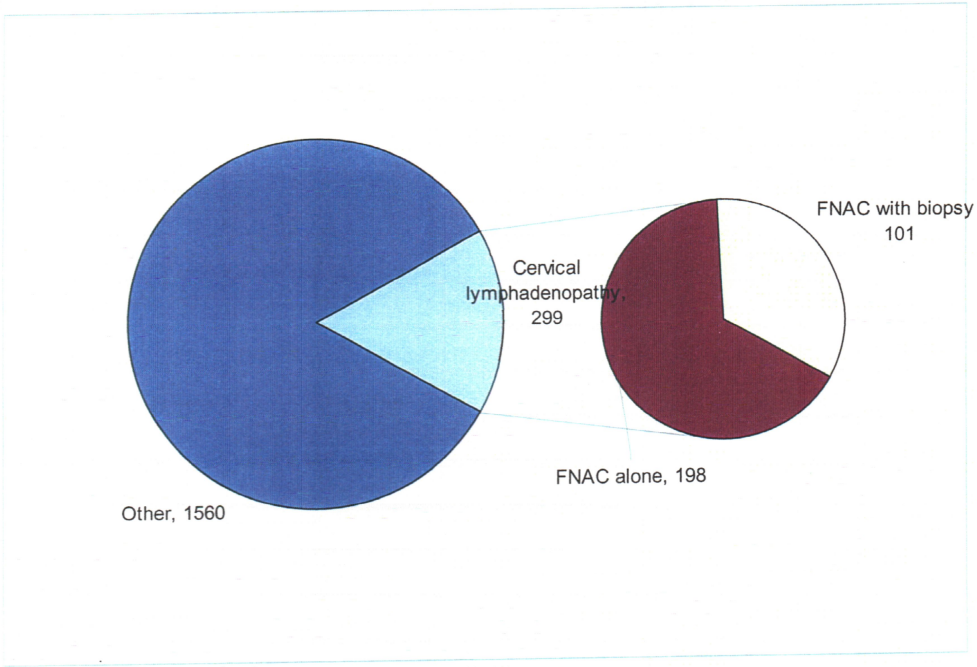
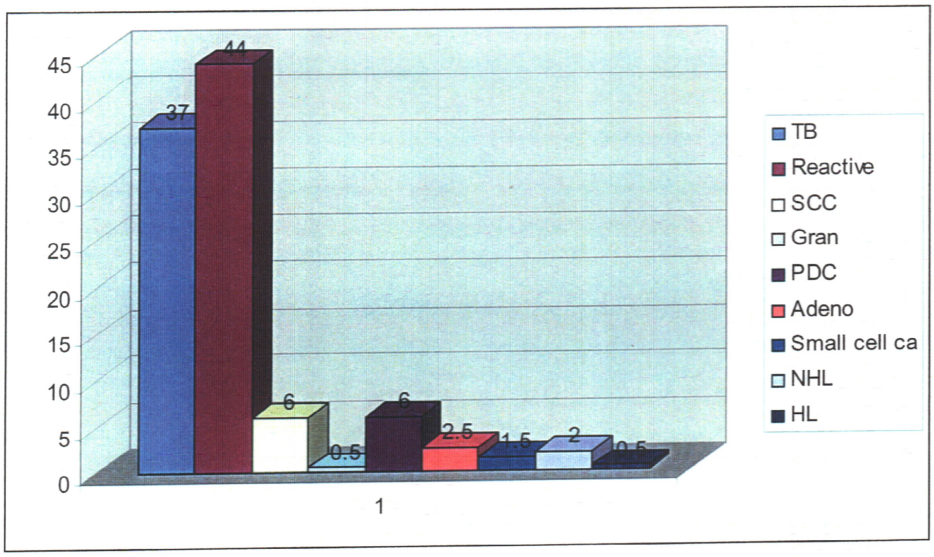
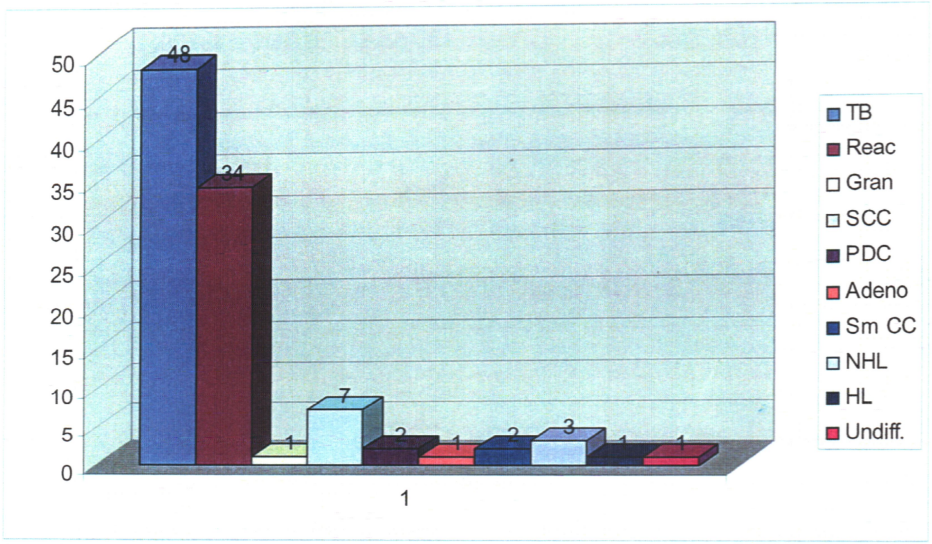


Figure 2: Frequency of diseases causing cervical lymphadenopathy diagnosed by FNAC:



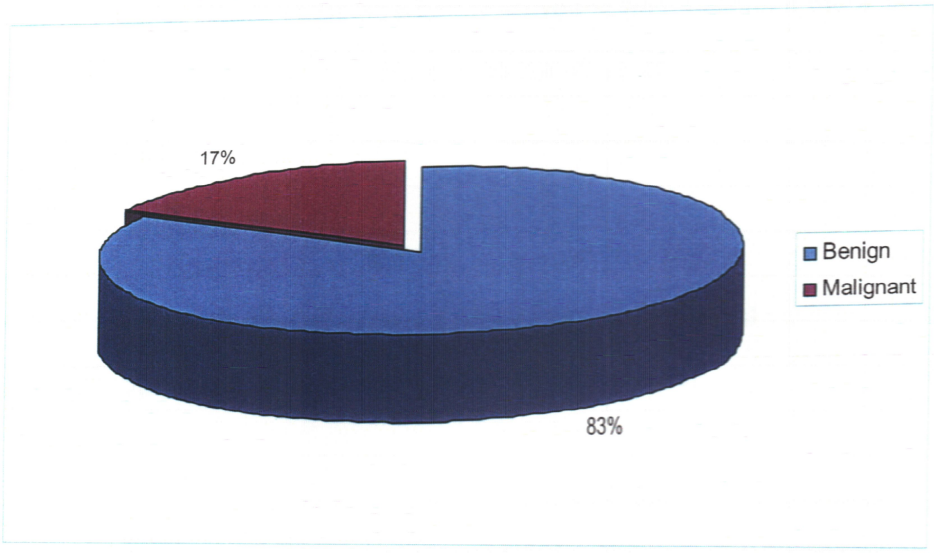
A total of 299 cases of cervical lymphadenopathy were diagnosed by FNAC. Reactive lymphadenitis was found to be more prevalent (44%) than TB lymphadenitis (37%).

Figure 3: Frequency of different diseases of cervical lymphadenopathy diagnosed by excisional biopsy:



Of the benign lesions Tuberculous lymphadenitis was the commonest (48 %), followed by reactive lymphadenitis and granulomatous lymphadenitis. Of the malignant conditions that metastasises to the cervical lymph node, squamous cell carcinoma was found to be the commonest (7%). Of the lymphomas, incidence of Non-Hodgkin's lymphoma were seen to be more than that of Hodgkin's lymphoma.

Figure 4: Distribution of benign and malignant conditions causing cervical lymphadenopathy diagnosed by biopsy:



In this study majority of the conditions were benign lesions comprising 83%. Malignant conditions constitute 17%.

Patients age ranged from 4 years to 68 years. The largest number of patients were in the age group 20-39, followed by age group1-19. It was observed that largest number of benign conditions , such as TB lymphadenitis and reactive lymphadenitis occurred at the age below 40 years, and malignant metastasis to cervical lymph node occurred in the age above 40 years.

Table 1: Age distribution of patients presented with cervical lymphadenopathy (in benign and malignant conditions):

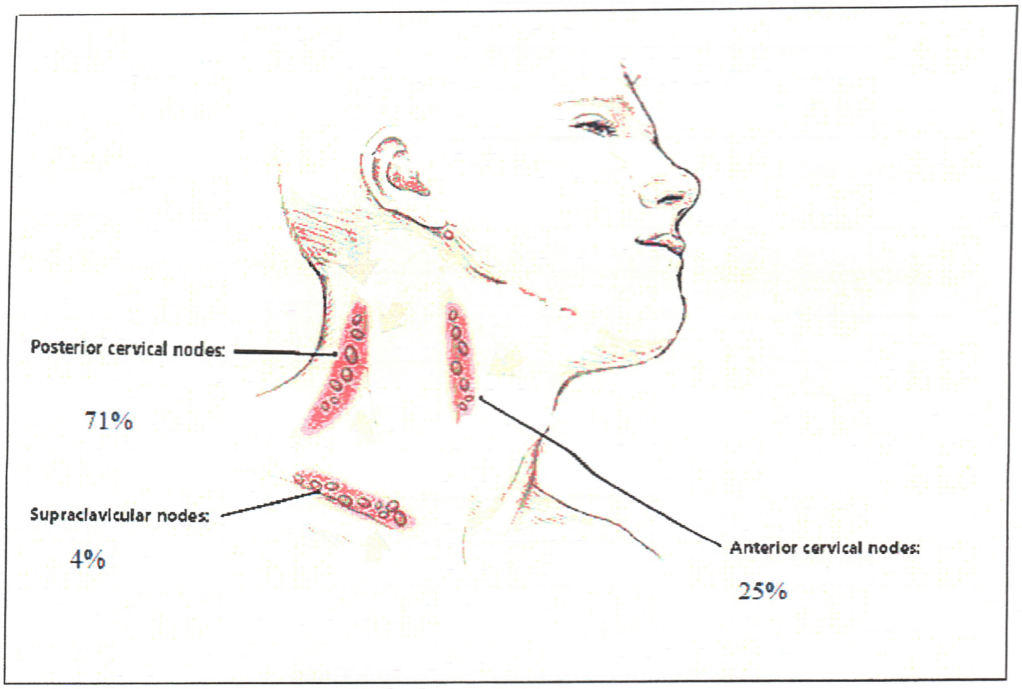
Age	Benign	Malignant	Total/Percentage
1-19 yrs	32	1	33 (32.60%)
20-39 yrs	44	0	44 (43.6%)
40-59 yrs	6	8	14 (13.9%)
60-79 yrs	2	8	10 (9.90%)
Total/Percentage	84 (83.2%)	17 (16.8%)	101 (100%)

Table 2: Sex distribution of patients presented with cervical lymphadenopathy

Sex	Benign	Malignant	Total/Percentage
Male	39	10	49 (48.5%)
Female	45	7	52 (51.5%)
Total/Percentage	84 (83.2%)	17 (16.8%)	101 (100%)

Male patients comprise of 48.5%, while female patients comprise of 51.5%, giving a male to female ratio of 1:1.

Figure 5: Sites of lymph node involvement:



Most of the patients presented with posterior cervical lymph node enlargement (71%), either single or multiple, followed by anterior cervical lymph node enlargement (25%) and only 4% presented with supraclavicular lymph node enlargement.

Table 3 : Site and side of lymph node involvement:

	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		
	Single	Multiple	Single	Multiple	Single	Multiple	Total/Percentage
Right	5	3	20	10	2	1	41 (40.6%)
Left	2	4	18	6	1	0	31 (30.7%)
Bilateral	0	12	0	17	0	0	29 (28.7%)
Total	7 (6.9%)	19 (18.8%)	38 (37.6%)	33 (32.7%)	3 (3.0%)	1 (1.0%)	101 (100%)

Most of the affected lymph nodes were present on the right side (40.6%), followed by left side (30.6%). Multiple, bilateral lymph nodes were enlarged in 28.7% patients.

The posterior group of lymph nodes were the most commonly affected group of lymph nodes on the right (30), left side (24), and even bilaterally (17).

Table 3 : Site and side of lymph node involvement:

	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		
	Single	Multiple	Single	Multiple	Single	Multiple	Total/Percentage
Right	5	3	20	10	2	1	41 (40.6%)
Left	2	4	18	6	1	0	31 (30.7%)
Bilateral	0	12	0	17	0	0	29 (28.7%)
Total	7 (6.9%)	19 (18.8%)	38 (37.6%)	33 (32.7%)	3 (3.0%)	1 (1.0%)	101 (100%)

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Table 4: Single lymph node enlargement in different sites and sides

Single LN enlargement							
	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		Total/Percentage
Disease	Right	Left	Right	Left	Right	Left	
TB LN	0	0	7	5	0	0	12 (25%)
Reac LN	1	0	13	11	0	0	25 (52.1%)
SCC	4	0	0	0	2	0	6 (12.5%)
SmCC	0	1	0	1	0	0	2 (4.2%)
PDC	0	1	0	1	0	0	2 (4.2%)
Adenoca	0	0	0	0	0	1	1 (2.0%)
Total	5 (10.4%)	2 (4.2%)	20 (41.7%)	18 (37.5%)	2 (4.2%)	1 (2.0%)	48 (100%)

Table 5: Multiple unilateral lymph node enlargement in different sites and sides

Multiple LN enlargement							
	Anterior cervical LN		Posterior cervical LN		Supraclavicular LN		Total/Percentage
Disease	Right	Left	Right	Left	Right	Left	
TB LN	2	2	9	5	0	0	18 (53.0%)
Reac LN	1	1	1	11	1	0	15 (44.1%)
SCC	0	1	0	0	0	0	1 (2.9%)
Total/ Percentage	3 (8.8%)	4 (11.7%)	10 (29.4%)	16 (47.1%)	1 (3.0%)	0 (0%)	34 (100%)

Reactive lymphadenitis was seen as the most frequent disease to present as

single lymph node enlargement, irrespective of the side of involvement. Whereas when multiple lymph node enlargement was encountered, TB lymphadenitis was seen to be the most frequent condition. Metastatic carcinomas were seen to involve all three groups of lymph nodes.

Table 6: Bilateral lymph node enlargement

	Bilateral/Multiple LN enlargement		
Disease	Anterior cervical LN	Posterior cervical LN	Total/Percentage
Tuberculous lymphadenitis	4	15	19 (65.5%)
Reactive lymphadenitis	3	1	4 (14.0%)
Granulomatous lymphadenitis	0	1	1 (3.4%)
Non-Hodgkin's lymphoma	3	0	3 (10.3%)
Hodgkin's lymphoma	1	0	1 (3.4%)
Undifferentiated carcinoma	1	0	1 (3.4%)
Total/ Percentage	12 (41.4%)	17 (58.6%)	29 (100%)

TB lymphadenitis was the most common cause of bilateral multiple lymphadenopathy, followed by reactive lymphadenitis and NHL.

Table 7: Duration of lymphadenopathy:

Disease	1-3 months	3-6 months	6-12 months	>12 months	Total/Percentage
TB LN	33	13	2	1	49 (48.5%)
Reactive LN	34	0	0	0	34 (33.6%)
Granulomatous LN	1	0	0	0	1 (1.0%)
SCC	0	1	6	0	7 (6.9%)
PDC	0	0	2	0	2 (2.0%)
Adenoca	0	0	1	0	1 (1.0%)
SmCC	0	2	0	0	2 (2.0%)
NHL	3	0	0	0	3 (3.0%)
HL	1	0	0	0	1 (1.0%)
Undiff ca	1	0	0	0	1 (1.0)
Total/Percentage	73 (72.3%)	16 (15.8%)	11(10.9%)	1 (1.0%)	101 (100%)

Of the benign conditions, most of the patients of TB (33%) and reactive lymphadenitis (34%) presented with lymph node enlargement during their first 3 months. TB lymphadenitis was also seen to have a longer duration (3-12 months) in 15% patients.

Most of the malignant conditions, in this study presented with lymph node enlargement, at 6-12 months time period, however lymphomas such as NHL, Undifferentiated carcinoma and Hodgkin's presented in the first 3 months period.

e of lymph nodes:

	<1cm	1-2cm	3-4cm	Total/Percentage
	0	23	26	49 (48.5%)
	1	31	2	34 (33.6%)
s LN	0	1	0	1 (1.0%)
	0	0	7	7 (6.9%)
	0	0	2	2 (2.0%)
	0	0	1	1 (1.0%)
	0	2	0	2 (2.0%)
	0	2	1	3 (3.0%)
	0	0	1	1 (1.0%)
	0	0	1	1 (1.0%)
ge	1 (1.0%)	59 (58.4%)	41 (40.6%)	101 (100%)

e TB lymphadenitis presented with multiple matted firm lymph

cm in maximum dimension. Reactive lymphadenitis

firm, discrete, single lymph nodes of 1-2 cm in maximum

ditions presented with hard fixed lymph nodes of

ension 3-4cm. Lymphomas had a rubbery architecture to the

Table 9: Correlation of FNAC with histopathologic diagnosis in cervical lymphadenopathy :

	FNAC	Histopathology									
		TB	Reac	Gran	SCC	PDC	AdenoC	SmallCC	NHL	HL	UndifC
TB LN	44	44	0	0	0	0	0	0	0	0	0
Reac LN	35	1	34	0	0	0	0	0	0	0	0
Gran LN	5	4	0	1	0	0	0	0	0	0	0
SCC	7	0	0	0	7	0	0	0	0	0	0
PDC	2	0	0	0	0	2	0	0	0	0	0
AdenoC	1	0	0	0	0	0	1	0	0	0	0
SmCC	2	0	0	0	0	0	0	2	0	0	0
NHL	4	0	0	0	0	0	0	0	3	0	1
HL	1	0	0	0	0	0	0	0	0	1	0

It was seen that 44 of the TB lymphadenitis cases correlated correctly with histopathology. However, 4 cases of histopathologically diagnosed TB lymphadenitis were reported as granulomatous lymphadenitis by FNAC and 1 case of histopathologically diagnosed TB lymphadenitis were diagnosed as reactive lymphadenitis on FNAC. Granulomatous lymphadenitis were thus taken as true positives for TB lymphadenitis , and the one case which failed to diagnose TB lymphadenitis on FNAC was taken as a false negative for TB lymphadenitis .

For cases of Squamous cell carcinoma, adenocarcinoma , poorly differentiated carcinoma, small cell carcinoma, and Hodgkins' s lymphoma, all cases of FNAC and histopathology were correlated correctly. One case of Anaplastic large cell lymphoma (NHL) Diagnosed on FNAC was diagnosed as undifferentiated carcinoma on histopathology, giving a false negative result. There were no false positive cases.

Sensitivity and specificity of FNAC in this study:

It was found that sensitivity was 98% and specificity was 100%.

Positive predictive value: 100%

Negative predictive value: 99.7%

Table 10: Sensitivity and specificity of FNAC in diagnosing benign and malignant conditions:

	FNAC	false negative	HPE	Sensitivity	Specificity
Benign	n=43	n=1	n=44	98.80%	100%
Malignant	n=16	n=1	n=17	94%	100%
Total	n=99	n=2	n=101		

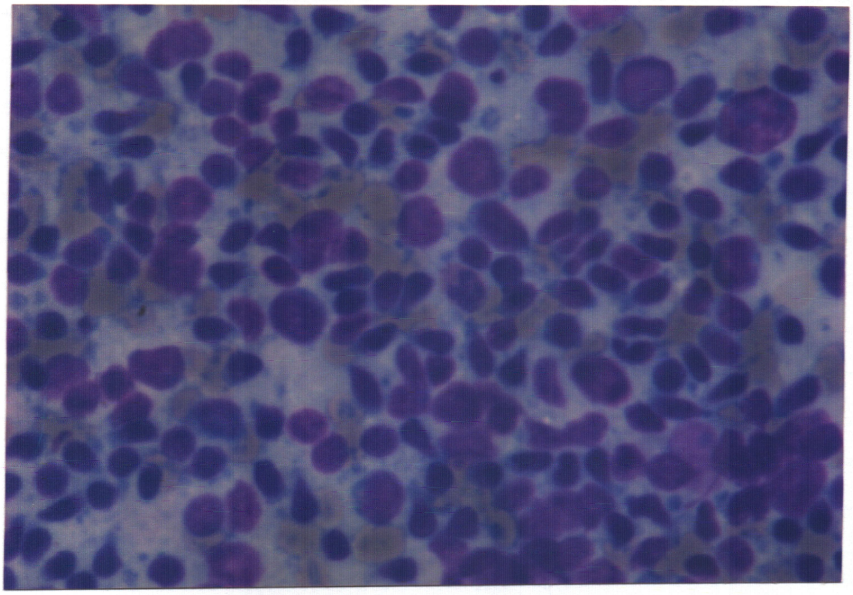

Fig 1: Reactive lymphadenitis, FNAC (Giemsa stain, x 400)

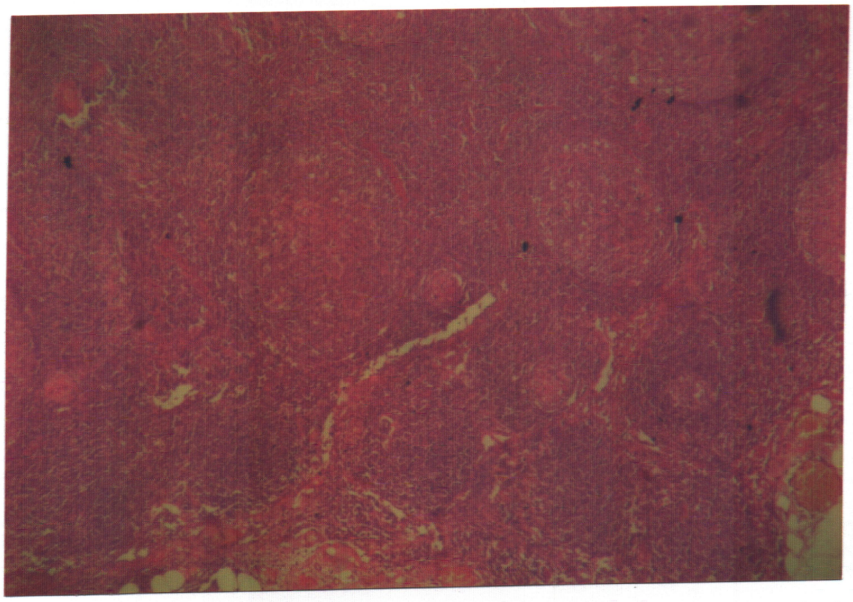

Fig 2: Reactive lymphadenitis, tissue section (H & E stain, x 100)

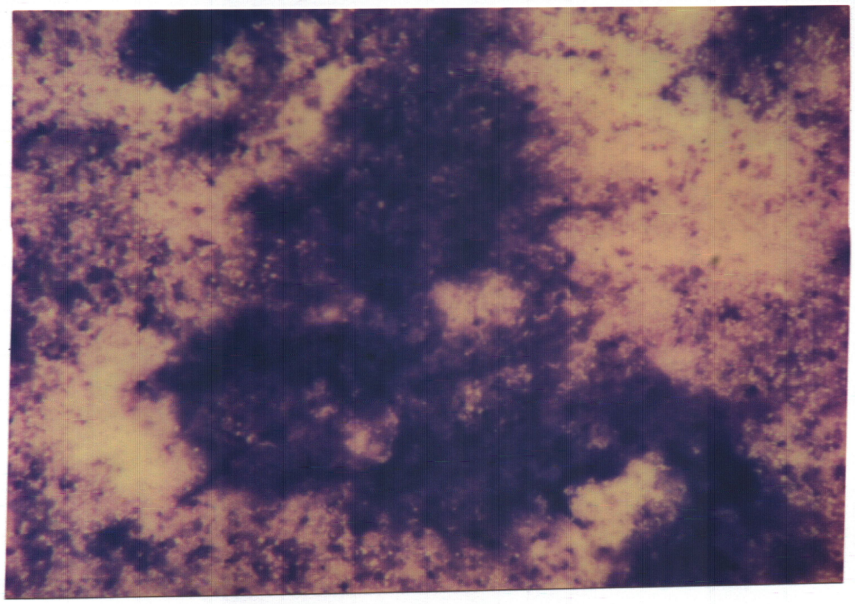

Fig 3: Tuberculous lymphadenitis, FNAC (Giemsa stain, x 100)

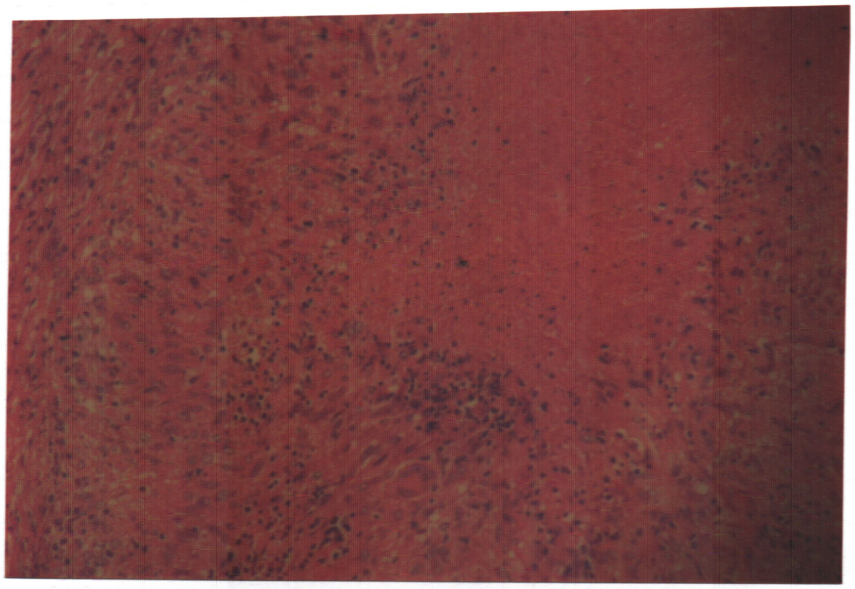

Fig 4: Tuberculous lymphadenitis, tissue section (H & E stain, x 100)

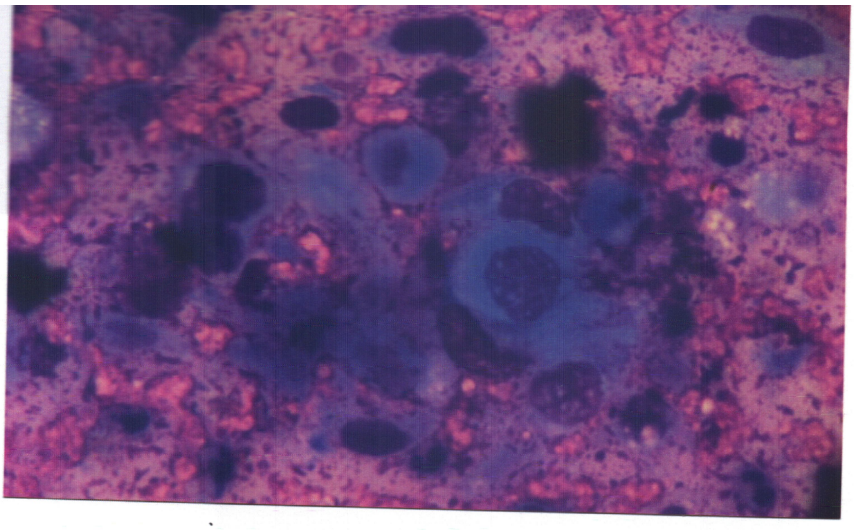

Fig 5: Metastatic squamous cell carcinoma, FNAC (Giemsa stain, x 400)

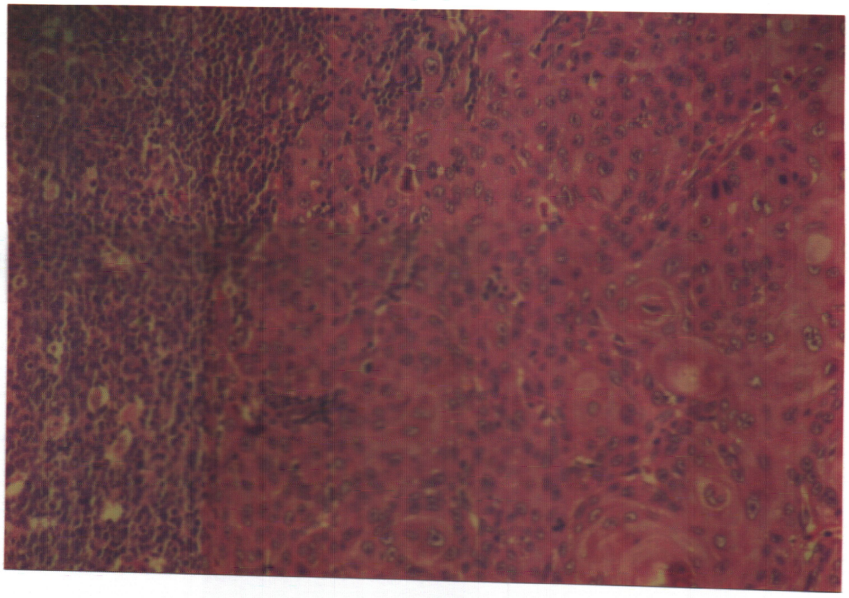

Fig 6: Metastatic squamous cell carcinoma, tissue section (H & E stain, x100)

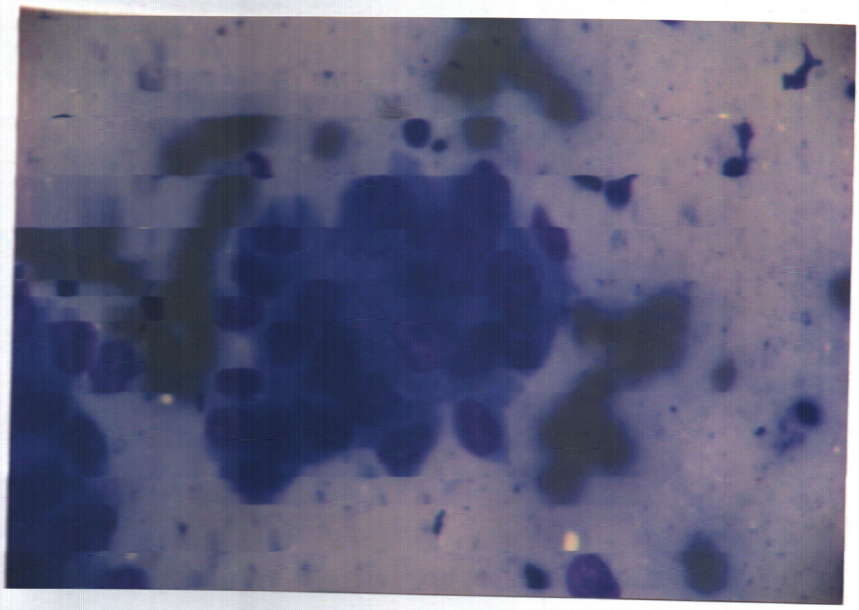

Fig 7: Metastatic adenocarcinoma, FNAC (Giemsa stain, x 400)

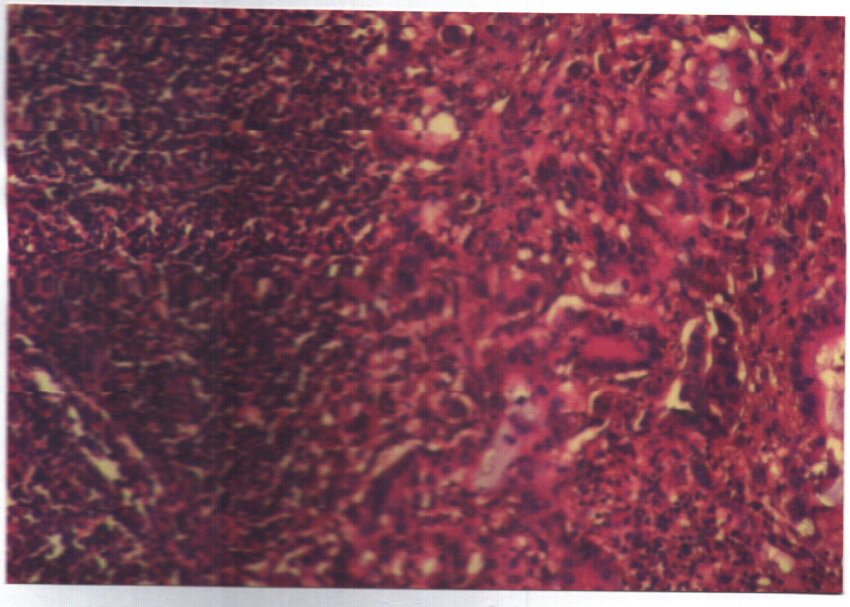

Fig 8: Metastatic adenocarcinoma , tissue section (H & E stain, x400)

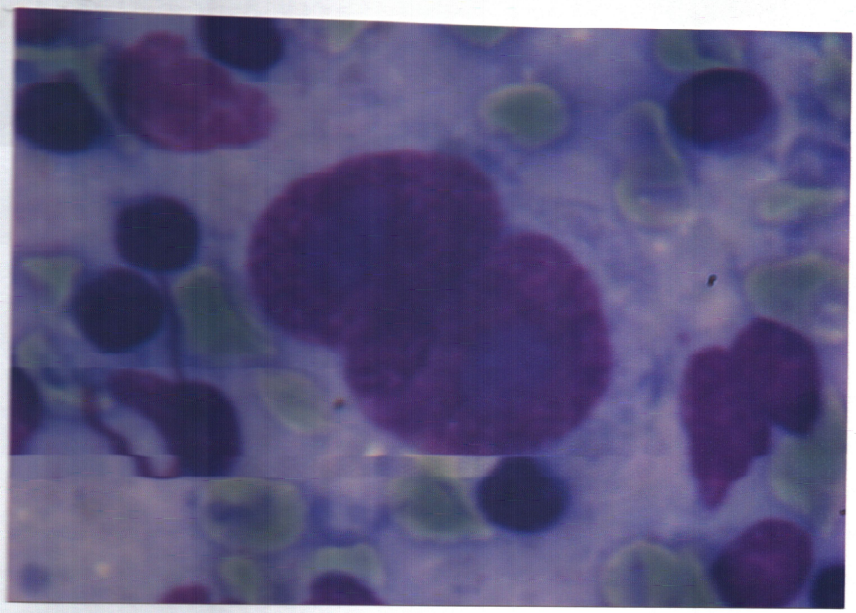

Fig 9: Hodgkin's lymphoma, FNAC (Giemsa stain, x 1000)

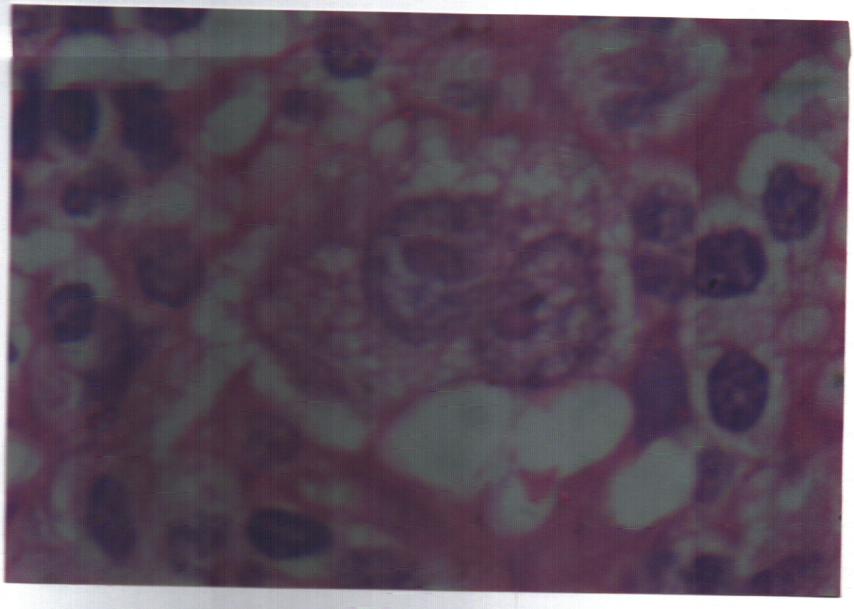

Fig 10: Hodgkin's lymphoma, tissue section (H & E stain, x1000)

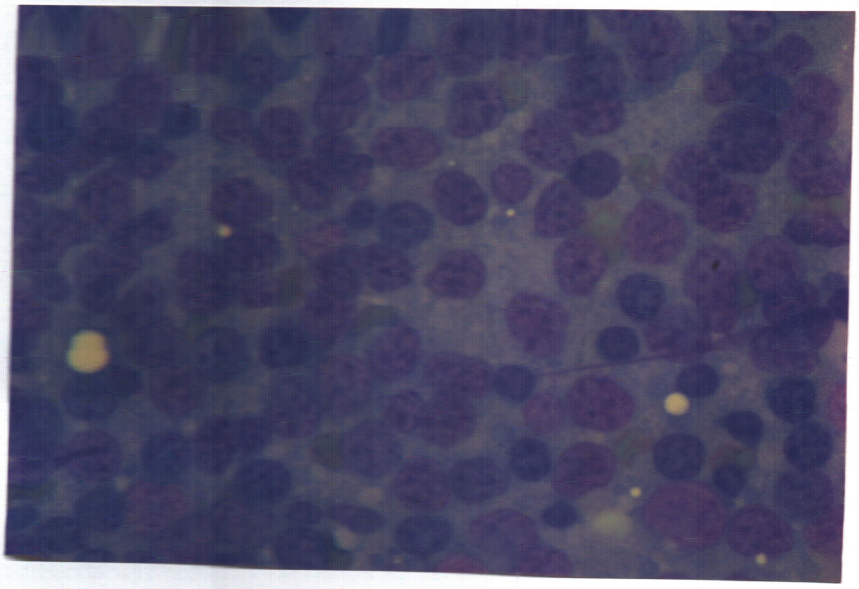

Fig 11: Non-Hodgkin's lymphoma, FNAC (Giemsa stain, x 400)

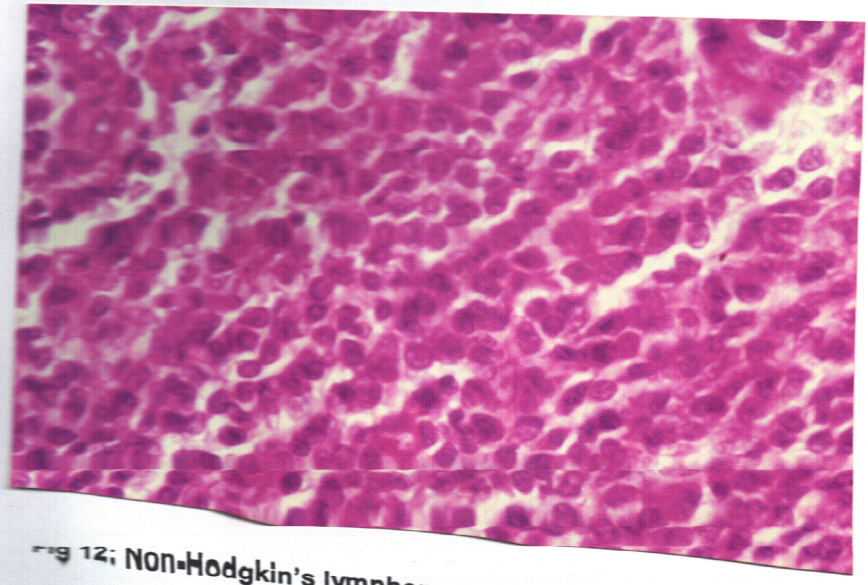

Fig 12: Non-Hodgkin's lymphoma, tissue section (H & E stain, x400)

DISCUSSION

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Discussion:

The use of fine needle aspiration cytology (FNAC) in the investigation of lymphadenopathy has become an acceptable and widely practiced minimally invasive technique, which is safe, simple, rapid and relatively pain- free. FNAC is highly cost effective and accurate as a first line investigative technique. In this study, FNAC of cervical lymph nodes were obtained from 101 patients who

Discussion:

The use of fine needle aspiration cytology (FNAC) in the investigation of lymphadenopathy has become an acceptable and widely practiced minimally invasive technique, which is safe, simple, rapid and relatively pain- free. FNAC is highly cost effective and accurate as a first line investigative technique. In this study, FNAC of cervical lymph nodes were obtained from 101 patients who presented with cervical lymphadenopathy. Cytological findings were analysed in correspondence to histopathological diagnosis of the same excised lymph nodes. Benign lesions were found to constitute of 83% of the enlarged lymph nodes, of which majority were tuberculous lymphadenitis, which constitute 48%, followed by reactive lymphadenitis, which constitute 34%, followed by one case of granulomatous lymphadenitis. These findings correlate with studies done by Nada. A. Alwan et al and Kiery J at el [42], who also reported benign conditions comprising majority of cervical lymphadenopathy 55.3% and 49.5% respectively. Taking in consideration the 299 fine needle aspiration cytology aspirations of cervical lymphadenopathies done through the whole year, reactive lymphadenitis constituted the majority of cases. This goes in accordance with study done by Nada et al. A possible explanation for this is that the study was performed in the Middle east where a high socioeconomic class population resides, where tuberculosis is not as prevalent as the Asian population. But however when the 101 cases were taken which followed biopsy, tuberculous lymphadenitis constituted majority of cases. Kiery J et al reported tuberculous lymphadenitis to be more common than that of reactive lymphadenitis. Malignant metastasis to the

cervical lymph nodes were seen to be more common than the primary neoplasms of the lymph node. This finding also goes in accordance with study done by Keiry J et al who reported that malignant metastasis to cervical lymph node were more common than primary lymph node neoplasms. Squamous cell carcinoma constituted most of the metastasis, primary being mostly of head and neck [43] followed by lung. These go in accordance with studies done by CS Nithya [44] who concluded oropharyngeal carcinoma to be the commonest to metastasize to cervical lymph nodes, most common being ipsilateral level II lymph nodes (63.6%), followed by involvement of level I lymph nodes (51.5%), level III(10.2%), level IV (15.2%). Shah et al had similar results. [34] This is not surprising as squamous cell carcinoma of the head and neck is one of the most commonest cancers worldwide. [45] Nodal metastasis is the most important prognostic factor , especially in squamous cell carcinomas of the head and neck. It decreases the overall survival by half. [46] The level of nodal metastasis and the number and size of nodes are also significant and these factors correlate with distant metastasis. The 5 year survival of patients in studies done by Nasser et al [47] was 25%.

There was no sex predilection, as male to female ratio is almost equal to 1:1 ratio. The largest number of patients were of the age group 20-39 years, followed by 1-19 years, and most of them were diagnosed as TB lymphadenitis. Tuberculosis is a communicable disease and young individuals are exposed in the external environment as they lead a more social life. [48] Malignant metastasis to lymph node occurred at the age range

60-79 years. These findings correlated with studies done by Pandit A. at el who also reported majority of cases belonged to age group 21-40 years, followed by age group 13-20 years, most constituting of benign lesions. Malignant metastasis to lymph node also were seen mostly in the older age group population. [49]

The posterior group of cervical lymph nodes were the most frequently enlarged, constituting 71% , followed by anterior group of lymph nodes and the least affected were the supraclavicular group of lymph nodes. Patients with reactive lymphadenitis mostly presented with single discrete, firm, mobile lymph nodes following history of sore throat, or fever. TB lymphadenitis patients mostly presented as multiple matted lymph nodes, involving right side and bilaterally. Both conditions involved posterior group of lymph nodes more frequently. These findings correlate with studies done by Kheiry J at el, who also reported mostly affected lymph nodes were from the posterior triangle , followed by upper jugular and supraclavicular groups.

Tuberculous cervical enlargement is due to the infection by tubercle bacilli either in the tonsil or in lung or both. The right sided bronchus is more wider, shorter and vertical. So that, probably TB infection is also more common on the right side, like other infections, and subsequently right sided lymph nodes could have been affected more than the left side. [20]

Metastasis to lymph nodes were mostly due to squamous cell carcinoma and involved the anterior and supraclavicular group of lymph nodes, and presented as hard, fixed lymph nodes of maximum dimension of 3-4 cm. Metastatic small cell carcinoma, poorly differentiated carcinoma presented as anterior and

posterior group of lymph nodes. Metastatic adenocarcinoma presented as single hard fixed supraclavicular lymph node.

The diagnostic accuracy of FNAC in the current study had a sensitivity of 97.9 % and a specificity of 100% for TB lymphadenitis . There is 1 false negative result which failed to diagnose TB on FNAC and instead was given as reactive lymphadenitis. This could be due to failure to aspirate from the area of caseous necrosis, where a more definitive diagnosis could have been given.

The most commonest cause of granulomatous lymphadenitis in this region is tuberculosis, therefore all cases of granulomatous lymphadenitis diagnosed on FNAC, subsequently diagnosed as TB on histopatholgy were taken as true positives. Nada A. et al reported a diagnostic accuracy of 79% for tuberculous lymphadenitis, while J Rawal et al reported a sensitivity of 95.8% and a specificity of 100%, which are similar to results obtained by this study. [50]

FNAC diagnosis of metastatic squamous cell carcinoma, poorly differentiated carcinoma, adenocarcinoma, small cell carcinoma and were correlated correctly on histopathology. Therefore FNAC has been highly accurate in the diagnosis of metastatic carcinomas of the lymph node.Three cases of Non-Hodgkin's lymphoma were correctly diagnosed by FNAC. Non Hodgkin's lymphoma, Hodgkin's lymphoma can be difficult to distinguish from metastatic nasopharyngeal carcinoma [51] , however it was correctly diagnosed in this study. One case diagnosed as anaplastic large cell lymphoma by FNAC was diagnosed as undifferentiated carcinoma on histopathology. It is stated that even on

histopathology biopsy alone, these two conditions are extremely hard to differentiate [52]. The sensitivity of this one case was therefore found to be zero. These findings correlated with findings of Pandit AA et al and Nada A. et al who found that the FNAC diagnosis of metastatic carcinoma to the lymph node were accurate with histopathogy. Their study included metastatic squamous cell carcinoma, adenocarcinoma, NHL and Hodgkin's lymphoma. FNAC was seen to provide an excellent cytomorphological picture in each of these cases, giving an accuracy rate of 96%. [53]The overall sensitivity was found to be 98%, and specificity was found to be 100% in this study. These findings are similar to studies done by Nada A. at el who reported their sensitivity to be 90.5% and specificity to be 98.8%. Another study done by Sarda at el reported an accuracy rate of 97%. [54]

CONCLUSION AND RECOMMENDATION

FNA cytology appears a well established as another adjunctive method of diagnosis, since its results compare favourably in many respects with those obtained from surgical biopsy. This fact is illustrated by the high sensitivity and specificity encountered in this study and others. In malignant lymphadenopathies, this inexpensive, relatively painless and rapid technique may not only help in the primary diagnosis of tumors, but remains a useful method of following up patients with known malignancies and even in guiding therapy.

Fine needle aspiration cytology is found to be a rapid and prompt way of finding out metastasis to the cervical lymph node and hence providing rapid treatment to the patient, therefore giving a good prognosis to the patient.

In this study a total of 101 cases were included in which excisional biopsy was done following fine needle aspiration cytology. Majority of cases included benign lesions (83%) followed by malignant conditions (17%). Reactive lymphadenitis constituted the majority of benign conditions (44%), followed by tuberculous lymphadenitis(37%). Squamous cell carcinoma from the head and neck region constituted the majority of metastasis to the cervical lymph nodes.

Fine needle aspiration cytology had a sensitivity of 98% and a specificity of 100%. Positive predictive value was found to be 97.9% and negative predictive value 100%.

Therefore FNAC can be used as a very reliable , accurate, cost effective , precise and friendly diagnostic procedure for determining diagnosis of cervical lymphadenopathies.

mendation

, effective and patient friendly procedure can be a useful tool in not only
ng the causes of cervical lymphadenopathy, but the prognosis of a
t diseases can take a toll by this simple procedure. Since it gives a high
rate, it can be used a reliable procedure.
ver in doubtful cases, correlation with histopathological examination is
nded.

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PROFORMA

Name: Case No:

Address:

Age:

Sex:

Clinical Details of lump:

Onset:

Site

Duration:

Associated pain:

Associated fever/ weight loss/night sweats etc:

Family history of TB/malignancy:

Relevant past history:

Clinical findings:

Site: right [ ] left [ ] bilateral [ ]

Anterior cervical [ ] Poterior cervical [ ] supraclavicular [ ]

Single [ ] Multiple [ ]

Size: <1 cm [ ] 1-2 cm [ ] 3-4cm [ ]

Consistency: Firm [ ] Hard [ ] Rubbery [ ] Matted [ ]

Mobile [ ] Fixed [ ]

Overlying skin:

Any other relevant findings:

Investigations:

CBC:

Mantoux test (if available):

Radiological findings (if available):

FNAC-

No.of dry slides:

No.of wet slides:

Special stains(if done)

Aspiration findings:

Diagnosis:

Histopathological Diagnosis:

Gross findings:

Outer surface:

On cut section:

Any relavant information:

Microscopic findings:

No. of slides H&E stained:

Any special stains required:

Diagnosis: