A STUDY OF ETIOLOGY AND CYTOMORPHOLOGICAL PROFILE OF SIGNIFICANT PEDIATRIC LYMPHADENOPATHY IN A RURAL TERTIARY CARE HOSPITAL

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INTRODUCTION

Lymph nodes are the encapsulated centers of lymphocyte differentiation and proliferation belonging to the class of secondary or peripheral lymphoid tissue.

Lymph node swelling is a common clinical condition in children which frequently poses a diagnostic dilemma for a pediatrician and concern for the parents. About 80% of children had palpable lymph nodes but only few are significant.[1]

The nodes have considerable capacity for growth and change, and with continued antigenic exposure, the lymphoid tissue continues to proliferate and enlargethrough puberty. As a part of the reticuloendothelial system lymph nodes serve as the termination point for lymphatic vessels that drain lymph from most tissues of thebody. Presence of abundant phagocytic cells, antigen presenting cells and lymphocytes provides ideal first line of defense against pathogens. As a result, mostof the normal children have palpable cervical lymph nodes[2]. If they are abnormally enlarged and, whether associated with serious underlying disease process, is theworrying point for the parents and the Pediatrician.

Lymphadenopathy is defined as an abnormality in the size, number or character of the lymph node[3,4]. Enlargement of two or more non-contiguous lymph node regions is known as generalized lymphadenopathy[5].

Regionallymphadenopathy is defined as the enlargement of lymph nodes within contiguous anatomic regions[6]. It occurs most often because of the presence of an infectious or inflammatory process in the region drained by the lymph node Majority of these are due to benign self limited disease secondary to viral or bacterial infections. However we have to rule out other serious systemic disorders and malignancy which are possible etiologies. The differential diagnosis of lymphadenopathy is broad. A thorough medical history and meticulous clinical examination is important in narrowing this differential. The distribution of the enlarged lymph nodes is important in the evaluation of lymphadenopathy in children. It may be due to systemic infections (viral, bacterial, fungal or protozoal), malignancies, autoimmune diseases, benign hyperplasia, drug reactions, histiocytoses and storage diseases among which the generalized lymphadenopathy due to systemic viral infection is the most common cause.

Lymph nodes should be examined for their size, distribution, character, mobility, accompanying cellulitis or periadenitis and presence of skin changes like raised temperature and erythema. Presence of organomegaly and signs of systemic disease should also be assessed.

Although the underlying etiology usually is a simple self-limited infection, more serious underlying etiologies including severe systemic illness, malignancies should be contemplated. Having an idea of region specific commonly encountered differential diagnosis is critical in directing an appropriate and timely evaluation. An organized approach is must to avoid an inappropriately rapid or over aggressive attempt at diagnosis or missing a serious disease.

Until recently lymph node biopsy was the investigation of choice for cases with lymphadenopathy, especially when malignancy is suspected. After the advent of fine needle aspiration cytology, it has been advocated as an alternative procedure in recent times. Over the years there has been an increase in the use of this technique. It is a simple, rapid, reliable, safe, cost effective technique with good diagnostic accuracy. It can obviate the need for surgical biopsy[7].

The dilemma to approach a child with lymphadenopathy, its evaluation and management, considering various differential diagnoses, stimulated us to take up this study.

AIMS AND OBJECTIVES

1. The objective of this study is to arrive at a definitive diagnosis in order to administer proper treatment.

2. To assess the clinical and cytomorphological correlation of significant lymphadenopathy in children from 6 months to 18 years of age.

3. To assess the etiological factors in assessing the pediatric significant lymphadenopathy.

4. To evaluate the role of FNAC in establishing the etiology of lymphadenopathy in children and to correlate cytological findings with clinical diagnosis.

REVIEW OF LITERATURE

Historical Review:

The ancient Greeks observed the lacteal vessels in the mesentery but could draw no useful conclusions from the observation.

The word lymphatic was used by Bartholin in 1653. William Hunter laid the foundations for modern knowledge of the anatomy and physiology of lymphatics.

Herophilus first noted lymph node enlargement and he named them as "Glandulae". Most of the early writers have called them "Glands', although there are no features to suggest as glands, because they have no glandular functions. Later Nermine anatomical adapted the term" Node for the lymph glands in 1955

Charaka, the ancient Hindu Physician had stated in his famous "Charakasamhitha", “If there is single swelling by the side of the neck it is called Galaganda. If these are many, they were called Galamala. They are regarded as curable, but are incurable if accompanied by coryza, pleurodynia, cough, fever.

Scrofula, the old name for surgical tuberculosis, in which adenitis is a common and striking variety, had been well known since the 5th century AD. It was supposed to affect any part of the body, the lymphatics and the lymphnodes being the primary site of the disease. The word scrofula is derived from the Latin word "Scrofo"which means a sow. It was probably so named either due to its occurrence in swine or the swollen neck of the patient, which mimics the large neck of the animals[8].

HISTORICAL ASPECTS OF FNAC

Kun first used the technique of aspiration cytology in 1847[9]. In 1905, the British Journal Memorandum carried an article published by Grieg and Gray about theaspiration of lymph nodes for the diagnosis of motile Trypanosomes. Around the same time, in 1907, Proscher employed the use of FNAC for the diagnosis of syphilis with the identification of Spirochetes from lymph node aspirates.

In 1901, Greig performed aspirations of lymphnodes to isolate the causative agent of Trypanosomiasis[10]. In 1921, Guthrie reported his results with aspirations using a 21- gauge needle and syringe. He successfully diagnosed cases of syphilis, Tuberculosis, Malignant lymphoma, Leukemia, Metastatic carcinoma by needle aspirations[11].

"Martin and Ellis in 1930 introduced the technique of needle aspiration biopsy[12]. Stewart in 1933 published the first report on aspiration cytology from New York and Cardazo analyzed the diagnostic accuracy of FNAC and it was upto 80%in various inflammatory and neoplastic lymph nodes [13,14].

Anatomy of Lymph nodes[16]:

Lymph nodes are encapsulated centers of lymphocyte differentiation and proliferation, belonging to the class of secondary or peripheral lymphoid tissue. A normal young adult body contains about 400-450 lymph nodes. The head and neck carry some 60-70 nodes, arm and superficial thoraco-abdominal wall upto umbilicus, have about 30 nodes, the leg, infra-umbilical abdominal wall and perineum have about 20 nodes. The remaining is divided between thorax about 100 nodes, and abdomen and pelvis about 230 nodes. Most richly served by nodes are gastrointestinaltract and tracheo bronchopulmonary tract.

Structurally the lymph nodes are small, oval or reniform bodies lying in the course of the lymphatic vessels. Each usually has an indentation on one side, thehilum through which blood vessels enter and leave. Efferent lymphatic vessel emergesfrom the hilum. Several afferent lymphatic vessels enter peripherally on the convex side of lymph node. Lymph node is covered by a capsule composed mainly ofcollagen fibers. From the capsule numerous dense connective tissues extend radially, dividing the node into lobules, known as Trabeculae. A network of fine collagen fibers known as reticulum permeates the spaces

enclosed in the capsule and trabeculae, and supports the various cells present within. Hilum has dense fibrous tissue, which may extend into medulla, with an efferent lymphatic vessel embedded within it. Arteries and veins supplying lymph nodes pass through hilum, give straight branches in the medulla and, in the cortex they form a dense arcade of arterioles and numerous anastamosing loops of capillaries.

Lymph nodes have a highly cellular cortex and medulla. Cortex is the outer zone surrounding the medulla. In the cortex the cells are densely packed and form isolated lymphoid follicles. The follicular center is composed mainly of cells, which are larger less deeply staining and rapidly dividing, and is known as germinal center. The cells produced in germinal center migrate to the surrounding outer layer knownas mantle zone, then to the sinuses and efferent vessel. In the medulla, the cells are less densely packed, forming irregular branching medullary cords containing numerous poorly demarcated cavities representing a network of minute lymphatic channels which drain into efferent lymphatic vessel at the hilum. The cortex is deficient at the hilum and the medulla reaches the surface here.

Under antigenic stimulation, the whole node reacts by increase in size and vascularity due to proliferation of cells like lymphocytes and macrophages, the number and size of germinal centers also increase.

Most of the cells in the lymph nodes are lymphocytes, both B- lymphocytes and T-lymphocytes are present. The distribution of lymphocytes varies in different regions. In the cortex cells are densely packed and form isolated lymphoid follicles that are composed mainly of B lymphocytes. The germinal centers of follicles constitute mainly of large lymphoblasts, the B-lymphocytes that have been stimulated by antigens, B- lymphocytes mature to plasma cells and are seen in the medullary cords.

T lymphocytes are found primarily in the area between the follicles and in the deep cortex (known as Para cortex). Macrophages also occur and are present mainlyin the walls of sinuses, medulla and, few within germinal centers. Other cells present are fibroblasts, endothelial cells, granulocytes, pericytes, smooth myocytes, follicular dendritic cells and myelinated nerve fibers.

Functions of lymph nodes[16]:

The juxtaposition of phagocytic cells, antigen presenting cells (APC) andlymphocytes in an area of sluggish blood flow in the lymphnodes provides the ideal environment as first line of defense against pathogens in the tissue fluid conveyed to them by the lymphatic & vessels. The essential roles of lymphnodes include:

1. The provision of a labyrinth of channels, of large volume and surface area, through which lymph slowly percolates.
2. The exposure of foreign material in the lymph to macrophages in nodal sinuses.
3. The trapping of antigen by different mononuclear phagocytes including dendritic types.
4. Production of lymphocytes and a pool of stem cells able to become antibody producing B-lymphocytes and mature T-lymphocytes.
5. Interaction between Antigen Presenting Cells (APC) and lymphocytes to produce an immune response, both cell mediated and humoral.
6. Re-entry of blood-borne lymphocytes into lymphatic channels and then to the haemal circulation.
7. Humoral antibody production and addition to lymph and to blood.

Topographical naming of lymph nodes[17]:

The lymph nodes in the body can be divided into the peripheral nodes and the deeper nodes. The peripheral nodes are superficial, which are generally easily palpable. The deeper nodes are associated with major vessels and viscera[18]. ThePeripheral nodes include the lymph node groups draining the head and neck, upper limb and lower limb.

Craniocervical nodes (Head & Neck)

These are divided into circular (Pericranio cervical ring and vertical chain of nodes.

I. Pericranio Cervical Ring : These are circular chain of lymph nodes present at the junction of the head with the neck, extending from chin to the external occipital protuberance bilaterally. These include:

Submental
Submandibular (with buccal nodes)

Retromandibular (with parotid)
Retro-auricular (or mastoid) Occipitalnodes.

These nodes drain the respective areas as suggested by their names and theefferent pass finally into the deep cervical nodes.

I. Vertical Chain

These are further divided into superficial and deep cervical nodes.

Superficial cervical nodes are further divided into anterior cervical and superficial cervical groups. Both the groups drain into deep cervical nodes.

Deep cervical nodes are arranged along, and embedded in or in areolar tissue near the carotid sheath. They consist of- Superior deep cervical nodes adjoin the upperinternal jugular vein.

One sub- group that is of importance is the jugulodigastric nodes, concerned with drainage of palatine tonsil. The efferents from these nodes drain to the inferior deep cervical nodes or, directly to jugular trunk. Inferior deep cervical nodes are related to the lower internal jugular vein, lying deep to the sternocleidomastoid. One node on or just above the intermediate tendon of omohyoid, the jugulomohyoid node is concerned especially with drainage of tongue.

Efferents from these nodes converge forming right and left jugular lymph trunk which on right side drain into the jugulosubclavian junction and on left side intothe thoracic duct. Lymph nodes in and anterior to the sternocleidomastoid muscle are designated as lying in the anterior triangle. Those deep cervical and superficial cervical nodes that lie behind the muscle are designated as posterior cervical nodes.

The deep cervical nodes. which lie just above the clavicle, are termed as supraclavicular or transverse cervical nodes.

Levels of Cervical Lymph nodes

Cervical group of lymph nodes have been divided into seven groups especially for the purpose of staging squamous cell carcinoma. This classification however, doesnot include the parotid, retropharyngeal and supraclavicular group of nodes.34

- Level I- Ia- Sub mental nodes
  Ib- Sub mandibular nodes
- Level II- Upper jugular nodes
  IIa- Anterior to IJV
  IIb- Posterior to IJV
- Level III-Middle jugular nodes
- Level IV- Lower jugular nodes
- Level V- Posterior triangle nodes
- Level VI- Anterior triangle nodes
- Level VII- Upper Mediastinal nodes

Etiology of lymphadenopathy[19,20]:

Generalized lymphadenopathy

I. Infectious

Viral: Epstein - Barr virus, Cytomegalovirus, Human immunodeficiency virusAdenovirus. Measles Rubella, Varicella, Hepatitis A through E viruses.
Bacterial: Septicemia, Brucellosis, Syphilis, Tuberculosis, Typhoid fever, Plague, Leptospirosis.

Fungal: Coccidiodomycosis, Histoplasmosis, Protozoal, Toxoplasmosis.

II. Non-infectious

- Malignancy: Hodgkin's disease (HD), Non-Hodgkin's Lymphoma(NHL), Histiocytoses, Metastatic Carcinoma, Acute stem cell leukemias, Neuroblastoma.

- Autoimmune Disorders: Juvenile Rheumatoid Arthritis(JRA) ,systemic lupus erythematosus (SLE), Serum sickness

- Drug Induced- Phenytoin, Allopurinol, Isoniazid

- Storage Diseases: Gaucher's disease, Niemann-Pick disease

- Endocrine Disorders: Hyperthyroidism, Adrenal insufficiency.

- Other Disorders: Chronic granulomatous disease, Acquired immunodeficiency syndrome, Sarcoidosis, Kawasaki.

Regional Lymphadenopathy[19,20]:

Regional lymphadenopathy can be the result of localized disease or a part ofor the first manifestation of generalized lymphadenopathy. Infections in the draining region are the commonest causes of regional lymphadenopathy.

Cervical:

Viral upper respiratory infections, Infectious mononucleosis, Rubella, Streptococcal pharyngitis, Staphylococcal pharyngitis. Tuberculosis, atypical mycobacterial infection, Toxoplasmosis, acute leukemia, lymphoma ,neuroblastoma Kawasaki disease ,BCG vaccination (BCG adenitis).

Occipital :

Pediculosis capitis ,Tinea capitis ,Secondary to local scalp skin infection,Rubella,

Preauricular:

Local skin infection, ophthalmic infection (ocuoglandular syndrome)Catscratch disease.

Submaxillary&Submental:

Oral and dental infections.

Supra clavicular:

Lymphoma, Tuberculosis ,Histoplasmosis ,Coccidiomycosis, intra abdominal, and intrathoracic pathologies.

Review of literature of Etiology of lymphadenopathy in children:

In 1977, Sheikh MM et al studied 183 children in the age group of 0-12 years with peripheral lymphadenopathy in Aligarh, India. Tuberculosis was the commonest cause found, in 49.2% of the cases, other causes were acute lymphadenitisin 28.9%. reactive lymphadenitis in 9.8%, and chronic non-specific lymphadenitis in 9.8%. and acute lymphoblastic leukemia in 1.1%, secondary metastasis in 0.5% and rheumatoid arthritis in 0,5% of the cases. Tuberculosis was common in 6-10 years agegroup and in female children[21].

Lake MA and Oski FA in the year 1978 studied peripheral lymphnodebiopsies over 10 year period in New York, USA. A total of 81 biopsies were performed on 75 patients aged between 18 months to 17 years. Of these patients 55% (41 cases) had nodes with non-diagnostic hyperplasia, 21%(16 cases) had non- caseating granulomatous lymphadenitis. 7% (5 cases) showed the caseating lesion of tuberculosis, while 17% (3 cases) showed lymphoreticular malignant neoplasm (Hodgkin's disease in 9 cases, other lymphoma in 3 cases and Histiocytosis-X in 1). Regional lymphadenopathy was seen in 70 patients (93.3%) and generalized lymphadenopathy in 5 patients (6.7%). Generalized adenopathy was associated with significant disease (lymphoma in 4 and mycoplasmal disease in l) in this series[22].

In a retrospective study conducted by Knight PJ et al, 239 children in the age group below 16 years who underwent lymph node biopsy were studied. A specific cause was found only in 41% of the cases, In 32% of the cases granulomatous disease was found, 13% had neoplastic diseases. 3% had chronic lymphadenitis, and in 52% of the cases causes could not be found. Causes for granulomatous diseases were catscratch .disease, tuberculosis and toxoplasmosis. Commonest neoplasm diagnosed was Hodgkin's disease. They opined that presence of symptoms like fever, loss of weight suggested the possibility of serious diseases[23].

Adelusola KA et al studied histopathological findings on 121 excised enlarged peripheral lymph nodes. Patients were in the age group of 9 months to 15 years. Cervical region was the commonest site (48%) involved. Tubereulosis, toxoplasmosis and histoplasmosis were seen in 44% of the cases. Non-specific lymphadenitis 31%) and malignant tumors (24%) were other causes[24].

In 1984. Mbise RL studied 257 excisional peripheral lymph node biopsies of children aged between four days and 15 years of age. The diagnoses made were tuberculous lymphadenitis in 67.3% of the cases, non-specific reactive lymphadenitis in 20.6%, malignant neoplasm in 13% and Histiocytosis-X in 0,8% cases,Tuberculosis was common below the age group of less than five years[25].

Kissane John M et al did a retrospective study of 100 peripheral lymph node biopsies over 15 years period. The diagnoses of these biopsies were acute inflammation in 9% of patients, granulomatous inflammation in 28%, and specific diagnosis in 26% (Hodgkin's disease, lymphocytic lymphoma, histiocytic lymphoma, malignant reticuloendotheliosis, metastatic tumor, eosinophilic granuloma), and hyperplasia or no diagnosis in 37% of the patients[26] .

Bhandari et al in their study performed 134 needle biopsies of peripheral lymph nodes in children aged 7 months to 15 years of age. The commonest cause of lymphadenopathy diagnosed was tubercular lymphadenitis in 50% of cases, followed by chronic lymphadenitis in 26.5%, acute pyogenic lymphadenitis in 59% and Hodgkin's disease in 1.4% of the cases[27].

Reddy MP et al studied 100 children with peripheral lymphadenopathy betweenthe age group of 1 month to 12 yrs in Mathura, India, in 1995. Tuberculosis wasfound to be the commonest cause of lymphadenopathy (35%). Other causes in orderof frequency were

chronic tonsillo pharyngitis (5%) cases). lymphoma 3% (Hodgkin's 1%, Non- Hodgkin's lymphoma-2%), AIDS (2%) and Infectious mononucleosis (1%),In 44% of the cases the cause was not determined even after detailed clinical, hematological, microbiological and radiological investigations (non-diagnostic reactive hyperplasia). FNAC was used as primary diagnostic test. Sensitivity and specificity of FNAC as compared to biopsy was 94% and 100% respectively[28].

Karadeniz C et al in Ankara, Turkey studied 382 patients in the age group 2 months to 16 years with peripheral lymphadenopathy. Majority (72%) of the patients was males, 19.1% of the patients had generalized lymphadenopathy. 36.1% had localized (one anatomic area involved) and 44.8% had limited (two or three areas involved). CMV, Infectious mononucleosis, Rubella, Acute leukemia, Non-Hodgkin'slymphoma frequently manifested with limited or generalized lymphadenopathy. Supraclavicular lymphadenopathy was associated with specific benign or malignant disease like malignancy in 20/27, tuberculosis in 3/27, CMV in 2/27, Sarcoidosis in 1/27 and lipoma in 1/27 of the cases with supraclavicular lymphadenopathy[29].

Benesch M et al in 1999 studied 87 children with peripheral lymphadenopathyand concluded that small, soft, mobile, non-tender, cervical, axillary or inguinal lymph nodes do not required further investigations. In case of enlarged, tender lymph nodes with overlying skin erythema and fever diagnostic evaluation should include complete blood count, erythrocyte sedimentation rate and or C-reactive protein level, supplemented by appropriate antibody testing (EBV, CMV, and Toxoplasma). Firm, enlarged, painless lymph nodes that are matted together and fixed to the skin or underlying tissues necessitate a more detailed diagnostic evaluation in order to exclude malignant or granulomatous diseases [30].

Soldes OS et al studied the predictors of malignancy in children with peripheral lymphadenopathy. Clinical factors that increased the likelihood of malignancy included the presence of fixed nodes. supraclavicular location. and an abnormal chest x-ray. Increasing node size, number of sites of adenopathy. and age allcorrelated with increasing risk of malignancy [31].

Dajani AS et al studied 34 consecutive cases of cervical lymphadenitis in children under 15 years of age. Throat cultures, nasal cultures and cultures of impetigious lesions on scalp or face were done. Needle aspiration was done for all the cases and sent for culture. Etiological diagnoses by all methods of diagnosis were Group A Beta hemolytic streptococcus in 74%

cases; staphylococcus aureus in 15 cases; mycobacterium tuberculosis, atypical mycobacteria and infectious mononucleosis each in 3% each: and cause was unknown in 2 cases. Only lymphnodes with size more than 3 * 3cm were included in the study[32].

Barton LL et al studied 74 children with cervical lymphadenopathy.Lymphadenitis was attributed to group A beta hemolytic streptococci in 26 of the patients, to staphylococcus aureus in 36% of the patients, both staphylococci and streptococci in 3s and peptostreptococci in 5%, other organisms isolated were Mycobacterium scrofulaceum (I3%) Pseudomonas (13%), fastidious gram-negative rod in (1.3%) and Franscicella tularensis (1.3%). In 24% of the children no etiologic agent could be identified[33].

Sundaresh HP et al studied 30 children under 17 years of age with cervical lymphadenopathy. Lymphadenitis was attributed to group A B-hemolytic streptococciin 33% of patients, to staphylococcus aureus in 13% of the patients, to infectious mononucleosis in 13%. In 3.3% of patients Mycobacteria was isolated and in another 3.3% cases Acinobacter. In 27% of the cases no etiological agent could be found 'From above studies it was seen that common etiological organism for acute Culture was negative in 24-35% of the cases[34].

Mishra SD and Garg BK studied 137 children with cervical lymphadenopathy.Of these, 77 cases (56.3%) were due to pyogenic infections (Acute or chronic tonsillitis in 32 cases, scalp infections in 28 cases, local trauma in10 cases and dental infections in 7 leukemia in 4 cases (2.9%), lymphosarcoma in 3 (2.2%), Hodgkins disease in 2 cases (1.4%), Infectious mononucleosis in l case (0.7%) and filarial in l case (0.7%)[35].

Moore SW et al evaluated the characteristics of surgically excised cervical lymphnodes in 1332 children less than 15 years of age in a developing country. 47.8%had non-specific reactive lymphoid hyperplasia and 36.3% had chronicgranulomatous changes. Tuberculosis was the leading cause of granulomatous changes (25% of cases). No mycobacteria other than M. tuberculosis were encountered. Pyogenic infections were identified in 32 cases (2.4%). 154 patients (1.7%) had neoplastic causes and Hodgkin's lymphoma was the commonest cause[36].

Connolly AAP and Mackenzie studied 360 children presenting with head and neck masses. Of these, 264 were non-lymphadenomatous benign lesions, 93 were lymphadenopathy masses and 3 were solid tumors. of the 93 children with lymphadenopathy masses the causes

determined on histology were reactive hyperplasia in 60 cases (64.6%). Mycobacterial infection in 21 cases (22.6%) and lymphoma in 12 cases (12.8%). Reactive lymphadenitis and lymphoma was common in male children and tuberculosis in female children[37].

'Fine needle aspiration cytology has been found to be a useful adjunct diagnostic technique especially in children. Over the years there has been an increase in the use of this technique It is a simple, rapid, reliable, safe, cost effective technique with good diagnostic accuracy. It can obviate the need for surgical biopsy and so, minimal trauma to the child with little to no morbidity. It can be done on outpatient setting with no need for admission and with no necessity for general anesthesia. The procedure also provides material for special studies like cytochemistry, culture, ultra structural examination and immunopathology[7].

Buchino JJ and Jones VF evaluated the use of fine needle aspiration cytology of enlarged lymph nodes in children. The aspirated material in 89.4% of the cases wasdeemed adequate for diagnosis. They found a sensitivity of 100%, a specificity of 97% and an accuracy rate of 98% for differentiating benign from malignant processes in peripheral lymph nodes. No significant complications were encountered[7].

Sarda AK et al in their study on FNAC concluded that it is reliable as theinitial evaluating procedure, it is cheap, speedy, easy to perform, with no complications, making it suitable for application in developing countries. Malignancy was correctly diagnosed in 100% and tuberculosis in 96% of the eases with the use of FNAC. Adequate material was obtained in 97.5% of the cases and overall accuracy rate was 97%[38].

Van De Schoot et al evaluated the role of FNAC in children with persistent or suspicious lymphadenopathy. Sensitivity and specificity of the procedure was 86% and 96% respectively. FNAC helped avoid additional surgical procedures in 86% cases. However, if FNAC showed malignant lymphoma, open biopsy was inevitable(8 of 13 cases) to establish proper classification[39].

Diagnostic accuracy for FNAC in tubercular lymphadenitis reported by different studies varied from 71% to 100%[40,41,42,43,44]. FNAC along with Mantoux test gave a diagnostic accuracy of 90% by Lau SK, et al[45]. FNAC along with ESR and Mantoux test gave a diagnostic accuracy of 97.72%[46].

Diagnostic accuracy by FNAC for leukemic infiltrates was shown to be 100% by Mondal A et al[47]. Diagnostic accuracy by FNAC for metastatic carcinoma was shown to be 73% by

Patra et al[48] and 97% by Mondal et al .

Pathogenesis of lymphadenopathy[17]:

The organisms reach directly by lymphatic flow from the inoculation site or bylymphatic spread from the inoculation site or by lymphatic spread from adjacent nodes. If initial involvement of regional nodes does not contain the infection adequately the organisms can reach non-contiguous nodes by hematogenous spread,.

Mechanism of lymph node enlargement:

i. Replication of cells within the node in response to antigenic stimuli or due to malignant transformation.
ii. Entry of cells exogenous to the node like neutrophils or metastaticneoplastic cells into the node.
iii. Deposition of foreign material in the histiocytic cells of the node asin case of lipid storage disorders.
iv. Release of local cytokines producing vascular engorgement andedema
v. Tissue necrosis within the node leading to suppuration .

Acute pyogenic lymphadenitis

The initial inflammatory response in the node, including complement activation and cytokine release, causes recruitment of neutrophils and mononuclear phagocytes. Rapid enlargement of the node occurs due to vascular engorgement and intranodal edema as well as cellular replication. Involvement of adjacent lymph nodesand surrounding soft tissues including skin. results in cellulitis, suppuration, necrosis and fixation to adjacent tissues. Lymph node architecture is destroyed once purulence occurs and it heals by fibrosis.

Sub acute or chronic granulomatous changes.

The increase in node size, tenderness and adjacent inflammatory response inthese cases are less impressive. Nodal architecture is destroyed due to formation of granulomas and in some cases caseating necrosis, requiring drainage to relieve pain and / or hasten resolution. With local or generalized viral infections the nodal response is primarily one of hyperplasia without necrosis that resolves without sequelae as infection abates.

Infectious causes of lymphadenopathy[17,19]:

Infections are the most common causes of lymphadenopathy.

Viral infections:

Lymph nodes associated with viral infections are usually small, soft and bilateral, without warmth or erythema of the overlying skin. Other associated symptoms are specific for the particular virus involved and are helpful in establishing a specific diagnosis.

Exanthematous viral infections:

Measles causes hyperplasia of all lymphoid tissue, with the lymph nodes at theangle of the mandible and in the posterior cervical region most commonly involved. Rubella is classically associated with tender posterior auricular, sub occipital and posterior cervical lymphadenopathy. These develop at least 24 hours before the onset of the rash and may remain for a week or more. The involved nodes are very tender to palpation. Other exanthematous viral illnesses include Varicella and Adenovirus infections.

Infectious mononucleosis syndromes: Infectious mononucleosis syndromes caused by Epstein Barr virus (EBV). Cytomegalovirus. Adenoviruses, Rubella and Hepatitis viruses, are usually associated with generalized lymphadenopathy.

Epstein-Barr virus causes 85-95% of mononueleosis syndromes, presenting with associated findings like fever, sore throat, rashes, malaise and fatigue. Tender enlarged cervical nodes are the hallmark and posterior cervical nodes are most often involved. Lymphnodes are enlarged singly or in groups, varying from 5 to 25mm in size, firm. freely movable and mildly tender to palpation. Hepatomegaly can be found in 10-15% of patients and splenomegaly in about half.

Cytomegalovirus produces mononucleosis syndrome similar to that due to EBV. Cervical adenopathy is less common in CMV (5%) than in EBV (95%) infection. Hepatitis viruses, especially Hepatitis B may also cause mononucleosis type symptoms associated with jaundice.

Adenoviruses may produce mononucleosis like syndrome, with generalized lymphadenopathy seen in 10-20% of patients. Pharyngoconjunctival fever characterized by fever, pharyngitis and conjunctivitis of acute onset, is the usual presentation. Cervical adenopathy is more frequent and hepatosplenomegaly is present in many. The anterior and posterior cervical nodes are enlarged in many patients. Acute respiratory disease due to Adenoviruses has generalized constitutional symptoms and localized respiratory symptoms with bilateral cervical adenopathy.

Acute HIV infection may present like mononucleosis syndrome with fever, malaise, myalgias, headache, sore throat, and diarrhea and maculopapular rash associated with lymphadenopathy in 50% of the patients. Lymphadenopathy may remain once acute symptoms have resolved as Persistent generalized lymphadenopathy (PGL. Nodes are distributed symmetrically and are discrete and non-tender and suppuration does not occur. Children with perinatally acquired HIV often have generalized lymphadenopathy at presentation.

Herpes simplex gingivostomatitis is characterized by enlargement of cervical sub maxillary and sub mental nodes, associated with fever, mouth ulcerations and gingival erythema. adenopathy in 31s of cases. Occipital, Posterior auricular and posterior cervical nodes are involved.

Bacterial Infections:

Bacterial infections causing generalized lymphadenopathy are uncommon. Disseminated bacterial infections may produce nodes that are painful, warm, tender and red. These nodes usually remain discrete and may suppurate or drainspontaneously. Bacterial sepsis or septic emboli associated with infective endocarditis may rarely result in generalized lymphadenopathy. Lymphohematogenous dissemination of Tubercle bacilli results in hepatosplenomegaly and generalized lymphadenopathy in about half of patients. It is usually

associated with mediastinal lymphadenopathy. Cervical region is common peripheral site involved. Generalized lymphadenopathy may also occur with other bacterial infections like syphilis, Brucellosis, Tularemia and Scarlet fever.

Bacterial infections are commonly associated with regional lymphadenopathy. In tonsillar and pharyngeal diphtheria, bilateral cervical lymphadenopathy is seen in many cases. Pneumonia due to mycoplasma pneumoniae, cervical adenitis is seen in 25 of patients. Staphylococcus aureus, Streptococcus pyogenes infections are commonly associated with acute unilateral cervical adenitis. other organisms like anaerobic bacteria: gram negative bacilli. Franscicellatularensis, Yersinia pestis, Nocardia brasiliensis. Staphylococcus epidermidis or alpha hemolytic streptococcialso cause it.

Staphylococcus aureus or streptococcus pyogenes infection accounts for 40% to 80% cases of acute unilateral cervical adenitis. The typical patient is 1-4 years of age with a history of recent upper respiratory symptoms (sore throat, earache, and coryza) or impetigo and has signs of pharyngitis, tonsillitis or acute otitis media. Infected nodes are usually submaxillary or superior deep cervical, 2.5 to 6cm in diameter, are moderate to intensely tender, and often are accompanied by erythema and warmth of the overlying skin. Systemic symptoms may be associated with cellulites or bacteremia occasionally suppuration and periadenitis is severe, withfluctuation seen in one third of the cases. Infection caused by S. aureus tends to have longer duration of disease before diagnosis. a higher likelihood of suppuration and slower resolution, clinical course and experimental data suggest that S.pyogenes is a primary cause and that staphylococcal infection usually occurs as a superinfection of a viral or streptococcal infection. In older children with acute onset of unilateral adenitis an anaerobic etiology secondary to periodontal or dental abscesses should be considered suggestive features are dental pathology, bull neck. severe inflammatory response, systemic toxicity and repeatedly positive blood cultures with isolation of Fusobacterium species or viridans streptococci. Some bacterial infections like Mycobacterial infections, catscratch disease and toxoplasmosis produce sub-acute or chronic lymphadenitis.

Tuberculosis of the superficial lymph nodes[49]

Striking enlargement of the superficial lymph nodes is an integral part of the primary tuberculosis complex. Involvement of the cervical nodes is most often the result of extension from the para tracheal nodes to the tonsillar and sub maxillary nodes or, from the apical pleurae and upper lung fields by direct spread to the inferior deep cervical (Supraclavicular) nodes. Rarely, they enlarge secondary to a generalizedadenopathy during the course of lympho hematogenous spread. Reactivation of quiescent tuberculosis infection can manifest initially as localized or generalized lymphadenopathy.

The tubercular nodes present in two clinical groups. The first, soon afterinfection as the nodes enlarge and are either still firm or beginning to soften. The second, much longer after infection, and often after a non-specific illness, when a calcified or partly calcified node breaks down to form an abscess. When superficial nodes are involved early in the infection enlargement is usually discrete, painless and the node is rubbery. Bilateral enlargement is the rule, but right- sided involvementmay predominate.

Acute non-tuberculous respiratory infections can precipitate or aggravate tuberculous lymphadenitis, resulting in local pain and perilymphadenitis. The primarynode is always the largest and those draining from it get progressively smaller. In general, younger the child the larger the nodes. Without treatment firm nodes tend to soften within six months of first appearance. Stages of tubercular lymphadenitis: In the first stage, the infection spreads by lymphatics to the nearest lymph nodes. At this stage nodes become simply enlarged without matting. In the second stage the enlargednodes become adherent to one another (matted) due to the periadenitis, This is the most characteristic feature of tubercular lymphadenitis. Later on caseation takes place in the interior of the nodes so that the nodes on become softer with gradual formation of cold abscess. This is the third stage. Gradually the cold abscess makes its way towards the surface and ultimately bursts forming a typical tubercular ulcer or a sinus.

Non- Tuberculous Mycobacterial infection:

Atypical mycobacterial infection occurs in children 1-4 years of age. Organisms are ubiquitous in soil and are probably ingested, and so the infection is localized to a submandibular or single tonsillar node. Bilateral involvement is rare. Initial appearance may be rapid with gradual increase in size over 2-3 weeks. Mostare 3 cm or less in diameter with minimal pain, tenderness or constitutional illness. About 50% of patients develop

fluctuant lesions and, 10% have spontaneous drainage and sinus tract formation. The skin changes from pink to a distinctive lilac red, with overlying skin developing a very thin parchment like quality. Signs and symptoms of M tuberculosis and atypical mycobacterial adenitis are identical, Chest radiography is normal and Mantoux tuberculin skin test has less than 15mm induration, usually 5- 9mm.

Bacillus Calmette-Guerin Vaccination:

BCG vaccination is associated with occurrence of lymphadenitis in about 0.5- 5% of cases. It is defined as the development of ipsilateral regional lymphnodeenlargement after BCG vaccination[50]. It may occur as early as two weeks aftervaccination but most of the cases appear within six months[51]. Ipsilateral axillarynodes are involved in 95% of the cases, supraclavicular or cervical nodes in others. Only one or two enlarged nodes are seen, with no tenderness or raised temperature over the swelling. Calcification and abscess formation with breakdown can occur in some cases, which can rupture and from sinus and heals by cicatrisation, Absence of fever, tenderness and other constitutional symptoms differentiates it from pyogenic adenitis. Cytopathology shows caseating granuloma formation. Acid-fast bacilli in smears or culture of Mycobacterium bovis from aspirated material are diagnostic[52].

Catscratch disease.:

Cat scratch disease is regional adenitis following inoculation of Bartonella henselae into skin or mucosal membrane. The most common sites of lymphadenopathy are the axilla (52%) and neck (28%), presumably from scratches onthe extremities and cuddling, respectively. Classically adenopathy begins 5 days to 2 months after inoculation (bite, scratch, exposure of mucous membrane). The affected node is generally solitary, often greater than 4 cm and tender. Constitutional symptoms are usually mild and include fever in upto 25%. Overlying skin is not red or warm but suppuration occurs in 30% to 50% of patients. Non-suppurative nodes diminish in size after 4 to 6 weeks.

Protozoal:

Toxoplasmosis Lymphadenopathy and fatigue without fever are the most common manifestations in symptomatic patients with acquired toxoplasmosis. Nodes commonly involved are cervical, sub occipital, supraclavicular, axillary and inguinal. The nodes are discrete, may or may not be tender, and do not suppurate. The adenopathy is localized or

involves multiple areas.

Fungal Infections:

Fungal and parasitic agents cause lymphadenopathy rarely even withdisseminated disease. Most often it is of a sub acute or chronic nature and the nodes are granulomatous and mildly tender. Histoplasmosis usually produces respiratory symptoms and hilar lymphadenopathy. When disseminated infection develops, especially in immune compromised patients, generalized lymphadenopathy is seen associated with hepatosplenomegaly, fever, endocarditis, pericarditis, and meningitis and bone invasion. Coccidiodes immitis infection primarily produces respiratory symptoms. When disseminated, it presents with generalized lymphadenopathy, meningitis, bony lesions and abscesses in about 0.5% of patients.

Non-infectious causes[19]

Malignancies:

Lymph node enlargement due to malignant disease is usually non-tender andis not associated with overlying erythema. The nodes may feel rubbery or hard, and groups of nodes may become matted together.

Hodgkin's Disease:

More than 90% of children with Hodgkin's disease have painless enlarged nodes in cervical or supraclavicular regions at presentation or occasionally in axillary and inguinal regions. The affected nodes are firm, non-tender with no evidence of regional inflammation. Constitutional symptoms like fever, anorexia, nausea, night sweats or weight loss may be present in about 1 / 3rd of these patients.

Non- Hodgkin's disease:

Various lymph node regions are involved in non-Hodgkin's disease depending on the histological subtype. Lymphoblastic NHL usually occurs in head and neck region or anterior mediastinum, small non-cleaved cell primary tumor arises abdomenand / or in head and neck, and large cell NHL primaries are usually painless masses arising from cervical lymph nodes or tonsils. FNAC or excisional biopsy of cervical lymph node establishes the diagnosis

Leukemia:

Generalized lymphadenopathy has been reported in 70% of children with acute lymphoblastic leukemia and in 30% of children with acute non-lymphoblastic leukemia. However this is usually an incidental finding and not the presenting complaint. The affected nodes remain discrete, rubbery and homogenous. On histological examination involved nodes are seen to be flooded by neoplastic cells. Diagnosis is by examination of the bone mamow, which is replaced by the leukemic lymphoblasts.

Metastatic carcinoma:

In Neuroblastoma, left supraclavicular nodes may be involved due to extension upward in the thoracic duct. Occasionally it may present with generalized lymphadenopathy. In disseminated form of histiocytic disorders generalized lymphadenopathy may occur associated with hepatosplenomegaly, seborrheic rashes, marrow failure, bony lesions and chronic otorrhea.

The nodes become enlarged, irregular and fined to the surrounding structures Important characteristic is, they are stony hard in consistency. Diagnosis is by biopsy and detection of the primary tumor.

Collagen vascular Diseases

Juvenile Rheumatoid Arthritis (JRA)

40% of children with JRA of systemic onset have generalizedlymphadenopathy, frequently preceding joint involvement splenomegaly and less often, hepatomegaly are present. Other manifestations include joint pains, rheumatoid rash, pleurisy, pericarditis, anemia, and abdominal pain.

Systemic lupus erythematosus (SLE):

70% of children with SLE have lymphadenopathy, which is generalized in onethird. cervical region is the commonly involved side. Manifestations include malaise, weight loss, growth retardation, fever, nephritis, musculoskeletal complaints, andpleural or pulmonary disease.

Storage disorders:

These are rare causes of lymphadenopathy. In Niemann-Pick and Gaucher's diseases lipid-laden macrophages accumulate in the lymphnodes, liver and spleen resulting in detectable enlargement.

Drug Induced:

Localized or generalized lymphadenopathy can appear 2 weeks afterbeginning Phenytoin or other anticonvulsion drugs. A severe pruritus, maculopapular rash with fever, hepatosplenomegaly, jaundice, anemia, and leucopenia are seen,

Other drugs implicated are Pyrimethamine, antileprosy and anti thyroid drugs, Isoniazid, Aspirin, Barbiturates, lodides, Sulfonamides ,Allopurinol, Tetracycline and Phenylbutazone. The symptoms abate after discontinuation of the drug.

Sarcoidosis:

This is a multi-system granulomatous disease of unknown etiology, Generalized lymphadenopathy with prominent cervical involvement is the most common finding in children. Nodes are discreet, painless and freely movable. Characteristic nodal histology is epithelioid cell tubercles with little or no necrosis. Biopsy of supraclavicular node is diagnostic in 85% of cases.

Kawasaki disease:

Lymph node enlargement is the least common of the principle diagnostic criteria of Kawasaki disease, and is seen in 50% to 75% of patients. Lymphadenitis is one of the earliest manifestations and is usually unilateral, confined to the anterior triangle, and the nodes are moderately tender, are usually greater than 1.5 cm diameter, non-fluctuant and there may be overlying erythema. Suppuration does not occur and resolution usually occurs early in the

course of the disease.

Cytopatholgy of lymphadenitis[53]

Non-specific reactive lymphoid hyperplasia:

In many instances the underlying cause of reactive lymphoid hyperplasia is not determined and it is a common diagnosis of lymphadenopathy. The most commonhistological pattern is that of follicular hyperplasia, in which well-delineated germinalcenters are prominent and are composed of a heterogeneous population oflymphocytes and tingible-body macrophages. A mixture of small lymphocytes and large lymphoid cells including immunoblasts are present with a complete spectrum of intermediate morphologic forms.

Suppurative lymphadenitis:

Aspiration smears in this condition are usually highly cellular and dominated by presence of large numbers of intact and degenerated neutrophils. Neutrophils are both dispersed and loosely aggregated. Bacteria may be seen both within phagocytes and extracellularly, especially with the Ramanowsky stains.

Tuberculous lymphadenitis:

The typical feature of tuberculous lymphadenitis is epithelioid cell granulomasassociated with necrosis. Epithelioid cells are modified histiocytes with a moderate amount of pale cytoplasm; a solitary nucleus with a characteristic elongated, bent or centrally indented shape, and small nucleoli. Syncytial arrangement of these cells results in granulomas, which are present in the background of necrotic, relatively acellular, homogenous debris. Multinucleated giant cells or Langerhans type with aggregated nuclei and copious cytoplasm are present in variable numbers.

BCG adenitis, which results due to vaccination with BCG, has similar cytomorphology as in tuberculosis but neutrophils and necrotic debris occur much more frequently with BCG disease.

Lymphoma:

Aspiration smear in Hodgkin's disease contains relatively low cellularity with polymorphous

lymphoid cell population in which small mature lymphocytespredominate and are mixed with eosinophils, plasma cells and often, histiocytes. Presence of Reid- Stemberg cells is characteristic of Hodgkin's disease.

Non-Hodgkin's lymphoma is characterized by high cellularity with presence of monomorphic population of lymphoid cells,

Diagnosis[6,19]

The evaluation of lymphadenopathy begins with thorough history and detailed physical examination with laboratory tests as indicated by these. The history should include the duration of lymphadenopathy. which is characterized as acute or subacute and chronic, the presence and duration of any associated systemic symptoms; any recent history of trauma or other infections in the region drained by the involved nodes, skin lesions, animal scratches or bites, any current medications: contact with persons infected with tuberculosis, medical and surgical history and family history.

Physical examination should include the location of the lymphadenopathy, measurement of size, number of involved nodes, characteristics of enlarged lymphnodes such as their shape, consistency, mobility, presence of tenderness, warmth, erythematous changes, fluctuance, firmness, adherence to adjacent structures and discrete or matted.

The physical examination should also include presence of signs of infection orinflammation in the region drained by involved nodes; signs of systemic disease, presence of hepatosplenomegaly, petechiae, purpura and echymosis

Findings in the history, physical examination that suggests a specific or uncommon diagnosis should direct the performance of additional or more specific laboratory tests. If the history and / or physical examination suggest a localized bacterial adenitis culture form possible primary focus is to be done and a course of antibiotics, which include Staphylococcal and Streptococcal coverage may be prescribed. A lymph node that is fluctuant, suggestive of acute bacterial lymphadenitis may be managed by fine needle aspiration, for diagnostic material, for culture that may direct antimicrobial therapy.

When the history and physical examinations are not suggestive of a malignant or systemic

condition, observation only with a follow-up may be the most reasonable course. If the lymphadenopathy persists, or the presentation is more worrisome, the initial diagnostic work-up should include a complete blood count with differential, erythrocyte sedimentation rate, placement of a PPD tuberculin skin test and a chest radiograph to evaluate for mediastinal adenopathy or pulmonary disease.

Serological tests for Syphilis, HIV. EBV, CMV infection, Brucella infection, toxoplasmosis, tularemia are done in suspected cases. If leukemia is suspected a bone marrow examination is done to confirm the diagnosis.

A lack of response to antibiotic therapy or, a dominant node that persist for sixweeks without identification of an infectious etiology warrants biopsy to exclude malignancy. When neither fine needle aspiration, serologic studies, skin tests. nor therapeutic trail of antimicrobial therapy are sufficient to confirm the cause of the infection or, to exclude a more serious cause and, when there is no decrease in the sizeof the node within 4-8 weeks of follow an excision biopsy should be considered.

Children with supraclavicular lymphadenopathy and children with persistent fever or weight loss with no specific diagnosis should undergo early biopsy. Because the majority of the cases of lymphadenopathy in children prove to be benign. Fine Needle aspiration cytology presents an attractive alternative to open biopsy. It is a rapid, simple, minimally invasive, cost effective diagnostic tool that does not require general anesthesia and has low morbidity.

Technique of FNAC[54]

The largest lymph node is selected. The selected lymph node is aspirated under strict aseptic precautions. Overlying skin is stretched and the lymph nodegrasped between the index finger and thumb of left hand.

A sterile 22- or 23-gauge needle is fitted to a 5-10 ml syringe and pierced obliquely into the lymph node. After entering the lymph node mass the plunger is withdrawn and the negative pressure created in the syringe the needle is moved back and forth several times with a constant suction. The negative pressure is released and the needle removed from the mass.

The needle containing the aspirated material is then detached, and air is drawn into the syringe. After reattachment of needle, content of the needle is ejected out on the clean, dry

and grease free glass slides smears are prepared using another glass slide exerting light pressure. The aspirate is examined for the amount and nature ofthe aspirated material, and then several smears are prepared. Excess of blood ifpresent, is removed using blotting paper. Caution is exercised to minimize the cell damage and preserve cell distribution.

Smears are immediately fixed in 95% ethyl alcohol, and stained by Haematoxylin and Eosin stain. Air-dried smears are also prepared and stained with wright's stain. Smears can also be stained with Zieh-Neelsen stain for the cases where necrotic material is aspirated or tuberculosis suspected, for the demonstration of acid- fast bacilli. Smears are examined under microscope for the cytological picture.

Treatment

Most cases of lymphadenitis in children are due to benign, self-limited causes ,which require very little diagnostic study and no specific therapy[20]. children with several nodes that are only slightly enlarged and minimally tender, in association withfew inflammatory signs, and serology is negative suggesting non specific etiology require only observation, following a wait and watch policy[4,55]. Some authors recommend the initial empirical use of antibiotics during early follow-up period. Mostsuch lymphnodes usually regress within 2-3 weeks. And most of the infectious causes are viral diseases, for which there is no specific treatment. When one or more lymph nodes continue to enlarge or does not regress even after 4-6 weeks, such children needfurther diagnostic evaluation.

Acute Lymphadenitis

Children with localized lymphadenopathy should be examined carefully for evidence of a primary focus such as pharyngitis, otitis media, skin infection or dental abscess and appropriate microbiological stains and cultures should be obtained to direct the antimicrobial therapy Most of the children common etiologic agents are staphylococcus aureus and streptococci and these will respond to empirical antibiotic therapy.

The initial choices of antibiotics are Penicillin-G or Amoxicillin and, Erythromycin if patient is sensitive to Penicillins. Subsequent change of antibiotic depends on the culture report and antibiotic sensitivity of the isolated organism. The average duration of therapy is 10 days unless abscess formation occurs. In this situation incision and drainage are indicated, and

antibiotics should be administered for 5-7 days after resolution of the acute process. Most common etiologic agents of acute suppurative lymphadenitis are S. aureus and Group-A Beta hemolytic streptococcus and empirical treatment should include antibiotic with actively against both of these organisms.

Parenteral therapy is beneficial in patients with marked lymph node enlargement, moderate to severe systemic symptoms and associated cellulitis[20].

Tubercular lymphadenitis:

The specific treatment for tuberculosis is with anti-tubercular drugs[56].

Treatment of local neck mass:

Whenever there is formation of cold abscess, which occurs following liquefaction of caseous and necrotic material, it is treated by incision scraping and excision of feeding lymph node. All the granulation tissue is scraped out and cavity is closed without keeping drain, to avoid formation of sinus. Excision of the sinus and surrounding skin along with feeding lymphnode is the treatment whenever there is sinus formation.

Mycobacterial lymphadenitis due to Atypical Mycobacteria

The preferred treatment of non-tubercular Mycobacterial lymphadenitis is complete surgical excision. Excision is more difficult if extensive caseation with extension to surrounding tissue has occurred and complication of facial nerve damage or recurrent infection is more likely. ATT is ineffective[17].

Toxoplasmosis:

Patients with lymphadenopathy secondary to toxoplasmosis do not need specific treatment unless they have severe or persistent symptoms or, evidence of damage to vital organs like chorioretinitis, myocarditis. If such signs and symptoms occur, treatment with pyrimethamine, sulfadiazine and leukovorin should be initiated.
Therapy is to be given lasts for at least 4-6 weeks. Loading dose of pyrimethamine for older children is 2mg / kg / day (maximum 50 mg) given for first 2 days. The maintenance dose is

1 mg/ kg / day (maximum 25mg / day). Folinic acid is administered daily depending upon the white blood cell count[58].

Catscratch disease:

CSD is usually self-limiting with resolution of regional lymphadenopathywithin 6-8 weeks. Antibiotic treatment of CSD is not clearly beneficial. Azithromycin, clarithromycin, rifampin, ciprofloxacin and gentamicin can be used. Suppurative lymph nodes that become tense and extremely painful should be drained by needle aspiration. Surgical excision of the node is rarely necessary[59].

BCG lymphadenitis:

Oral erythromycin, isoniazid and rifampicin have been used in the treatment of BCG lymphadenitis. However, controlled trials have indicated that these drugs neitherreduce the risk of suppuration nor shorten the duration of healing 'Since non- suppurative BCG lymphadenitis is a benign condition, and drugs do not alter itscourse but can have adverse effects, reassurance and expectant follow-up is all that is required[60].

Needle aspiration is recommended to prevent spontaneous perforation with sinus formation in suppurative BCG lymphadenitis, surgical excision may be needed when needle aspiration has failed [61].

Malignancy Hodgkin's disease[62]

The treatment depends on the stage of the disease. Both radiation and chemotherapy are highly effective in the treatment of Hodgkin's disease. The goal is to achieve cure while lessening treatment toxicity. For localized disease (stage I and Ila) radiation to standard fields with doses of 3500-4400 cGy may be the treatment ofchoice.

Multiagent chemotherapy with Nitrogen mustard, Vincristine (Oncovin), Procarbazine and Prednisolone (MOPP), or Doxorubicin (Adriamycin), Bleomycin, Vinblastine velban), Dacarbazine (ABVD) regimen is used, or

Alternating non cross-resistant regimens (MOPPl / ABVD) in combination with low dose (2000-2500 cGy) radiotherapy is used. This approach is recommended because potential growth defects and the risk of solid tumors are reduced by limiting the radiotherapy dose and

volume; risk of infertility and leukemogenesis is decreased by reduced exposure to alkylating agents and exposure to cardiopulmonary toxic drugs is limited.

MOPP regimen

Mechlorethamine

Vincristine

Procarbazine

Prednisolone

Usually six courses are given or, two courses beyond complete remission

ABVD regimen:

Doxorubicin .

Bleomycin.

Vinblastine .

Dacarbazine

Non-Hodgkin's lymphoma[63]

With development of effective multiagent chemotherapy most children with NHL are cured. Treatment regimens used are

COPP regimen:

Cyclophosphamide

Vincristine

Procarbazine

Prednisone

Cycles are l4 days with a 14 days rest period.

CHOP regimen

Cycloposphamide

Doxorubicin

Vincristine

Prednisone

Leukemia[64]

Acute lymphoblastic leukemia

The treatment of standard risk patients includes administration of induction chemotherapy, until the bone marrow no longer shows morphologically identifiable leukemic cells; prophylactic treatment of CNS and, continuation chemotherapy. Patients with standard or average risk of relapse are

- Between the ages of 1 to 10 years
- WBC count below 1,00,000 / mm3
- Lack of evidence of mediastinal mass or CNS leukemia
- B-progenitor cell immunephenotype.

Treatment plan is as follows:

Remission induction (4-6 wks) with Vincristine, Prednisolone, Asparginase. Intrathecal treatment with Methotrexate.Six cycles every week during induction therapy and then every 8 weeks for 2 years. Systemic continuation therapy with 6-Mercaptopurine and Methotrexate.

MATERIALS AND METHODS

SOURCE OF DATA

The study was conducted on children from 6 months to 18 years attending the outpatient department or admitted for inpatient care with significant lymphadenopathy at Adichunchanagiri Institute of Medical Sciences and Research Hospital, a rural tertiary care hospital, B.G.Nagara, Nagamangla Taluk, Karnataka over a period of 18 months (December 1 2014-May30 2016).

METHOD OF COLLECTION OF DATA

Inclusion criteria:

1. Patients in the age group of 6 months to 18 years.
2. Patients with significant lymphadenopathy

   Lymph node measuring >1 cm in cervical and axillary region.

   >1.5cm in the inguinal region

   >0.5 in the peripheral region
3. Lymph nodes which are rubbery or hard or with discharging sinus.
4. Matted lymphnodes of any size.

Informed consent was obtained from the parents/guardian to be included in the study.

Exclusion criteria :

1. Child with serious illness and systemic complications.
2. Children of age less than six months and adults greater than 18 years
3. Children of parents/guardian who refused to give informed consent.
4. Failure to thrive, Protein Energy Malnutrition (PEM).

Informed consent was taken from the parents/guardian for the inclusion. The clinical and laboratory data of the patient were recorded on a structured proforma.

The history of the child was taken in detail with reference to onset, duration ofswelling, whether associated with pain, sore throat, ear discharge, presence of skin lesions, associated systemic illness, history of allergies, contact with TB and exposureto pets, nutritional and

Socio Economic history was also recorded.

Thorough physical examination was done on each subjects including anthropometry, presence of pallor, skin lesions, throat examination and vitals were recorded.

Examination of all the group of lymph nodes were done in detail regarding location, number, size, consistency, surface, mobility and fixation. The areas drained by enlarged nodes were examined thoroughly for the focus of infection.

Significant findings of the systemic examination were also noted.

For all the study cases complete blood picture , Urine routine examination , peripheral smear, ESR ,Mantoux test , Gastric aspirate for AFB ,FNAC of the prominent lymph node were done. Chest X Ray, swab culture at source of infection, open biopsy of the nodes was performed in relevant cases.

Statistical Analyses:

Data was entered in MS Excel sheet and analyzed using SPSS software version 20.Descriptive statistics like mean, standard deviation were used after the values were expressed in percentages and in the form of tables and graphs.

Chi-Square test was used to check the association and P value < 0.005 was considered statistically significant at 95% confidence interval (CI).

Fig 1: Child with acute suppurative cervical lymphadenitis.

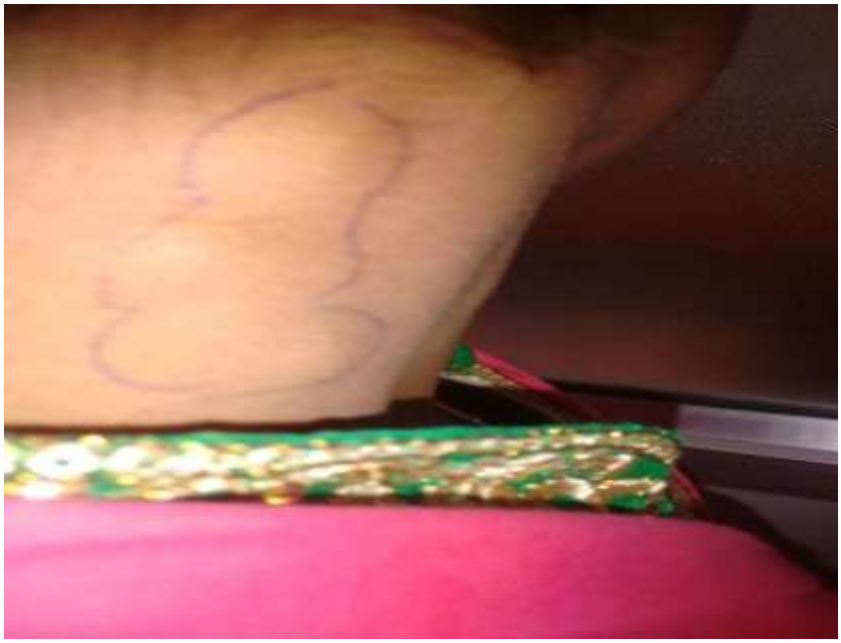


Fig 2: Child with matted lymph nodes in Tuberculous lymphadenitis.

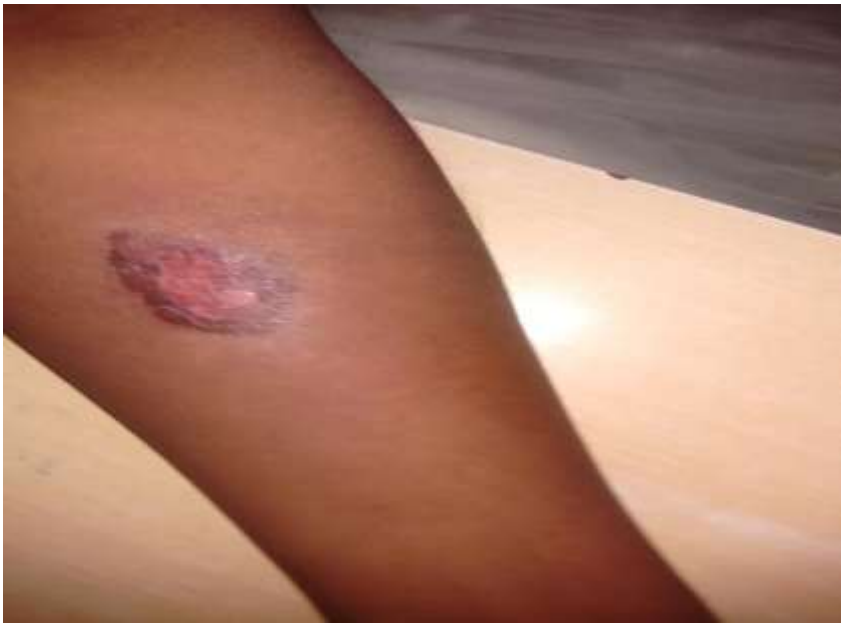


Fig 3: Strongly positive Mantoux test (ulceration) in a tuberculous lymphadenitis child.

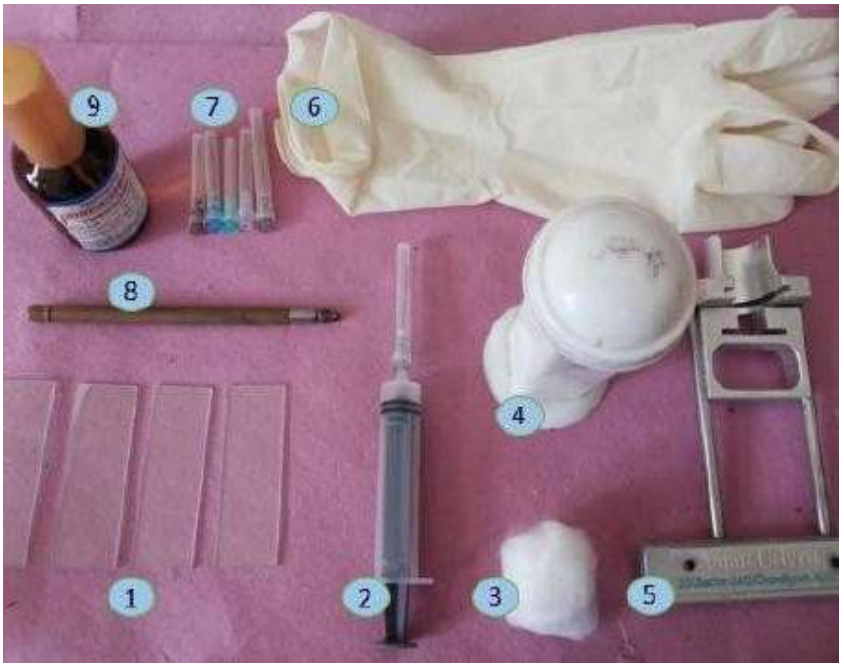


Fig 4: Instruments for FNAC procedure - *1. Slides 2.Syringe 3.Spirit swab 4.Koplin jar containing 95% Ethyl alcohol fixative 5.Franzen handle 6.Gloves 7. 22- 26 gauge needles, 8.Glass marker 9.Spray fixative*

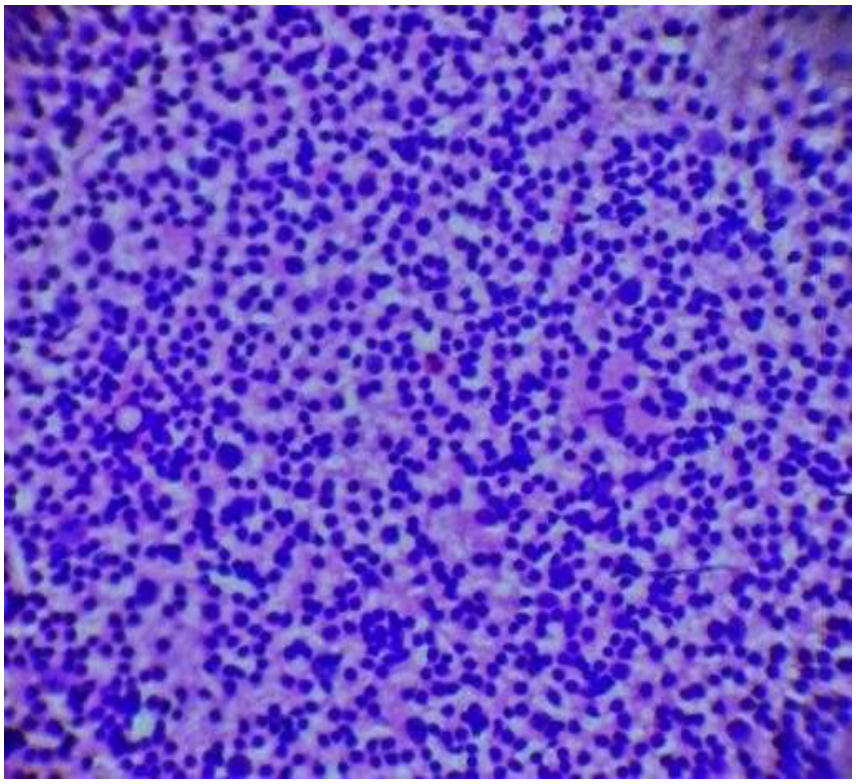


Fig 5 : Smear showing suppurative lymphadenitis.

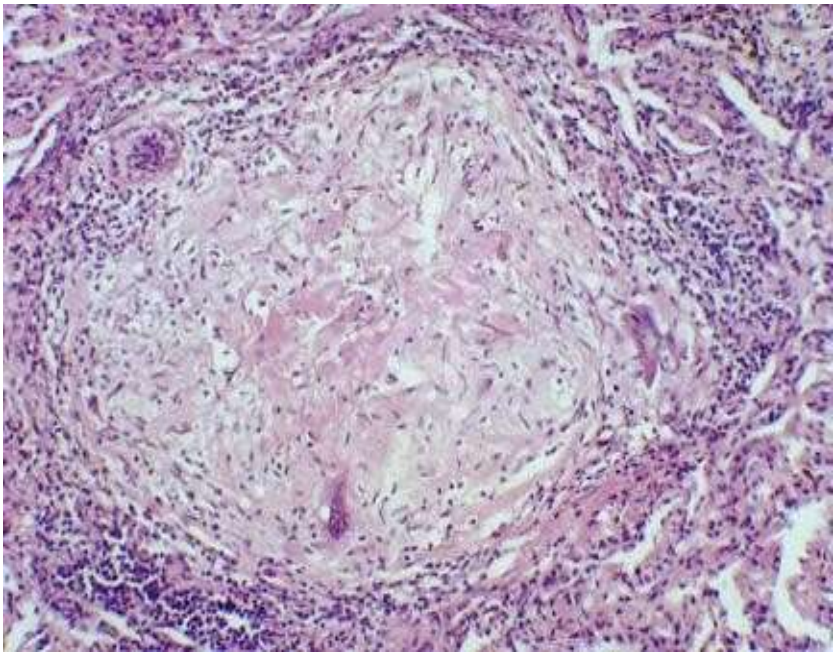


Fig 6: Histo pathological picture of caseating granulomatous lymphadenopathywith Langerhans giant cells.

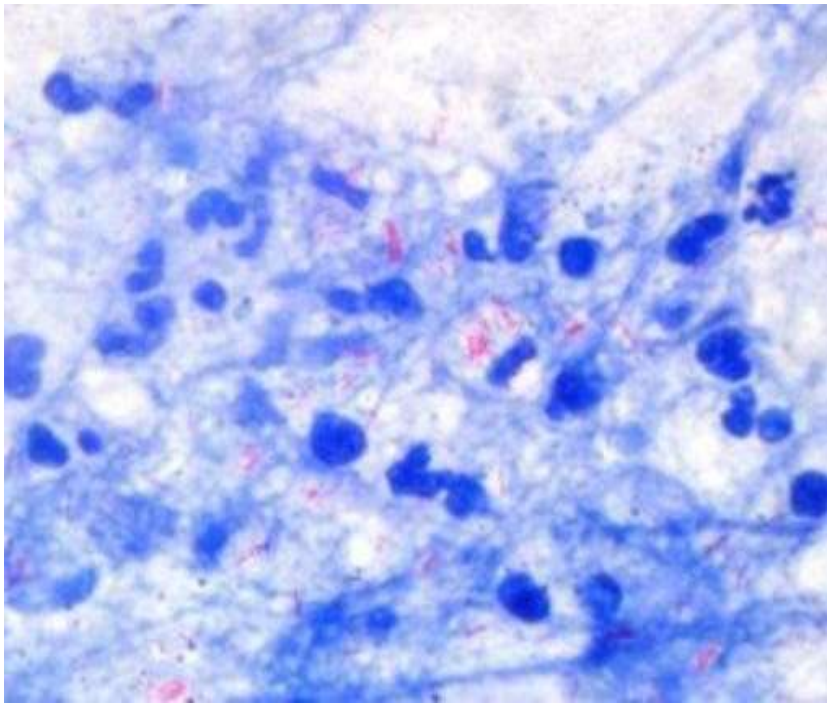


Fig 7: Acid Fact Bacilli (AFB) in FNAC smear.

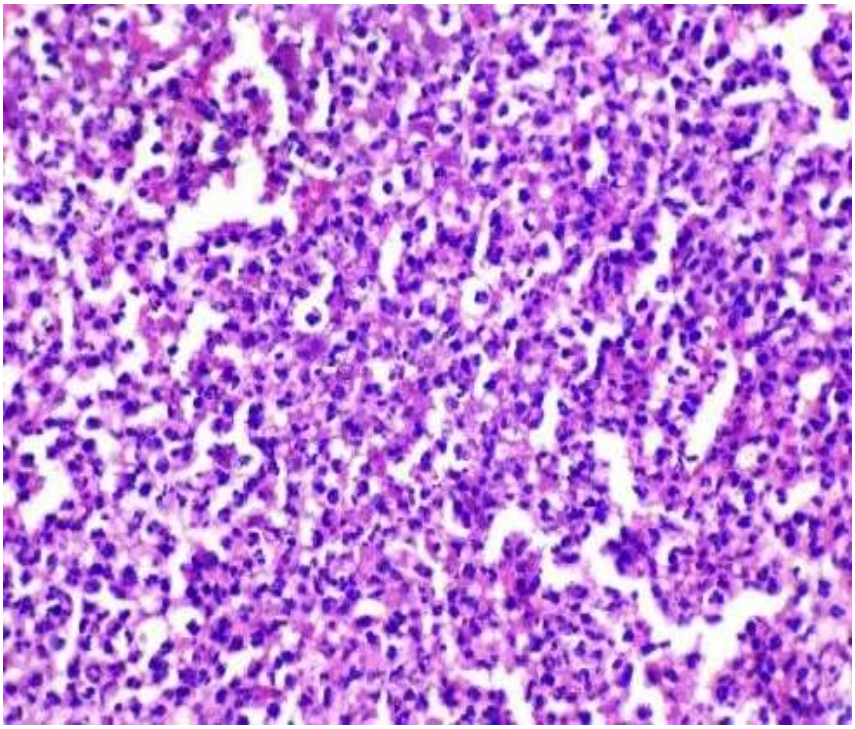
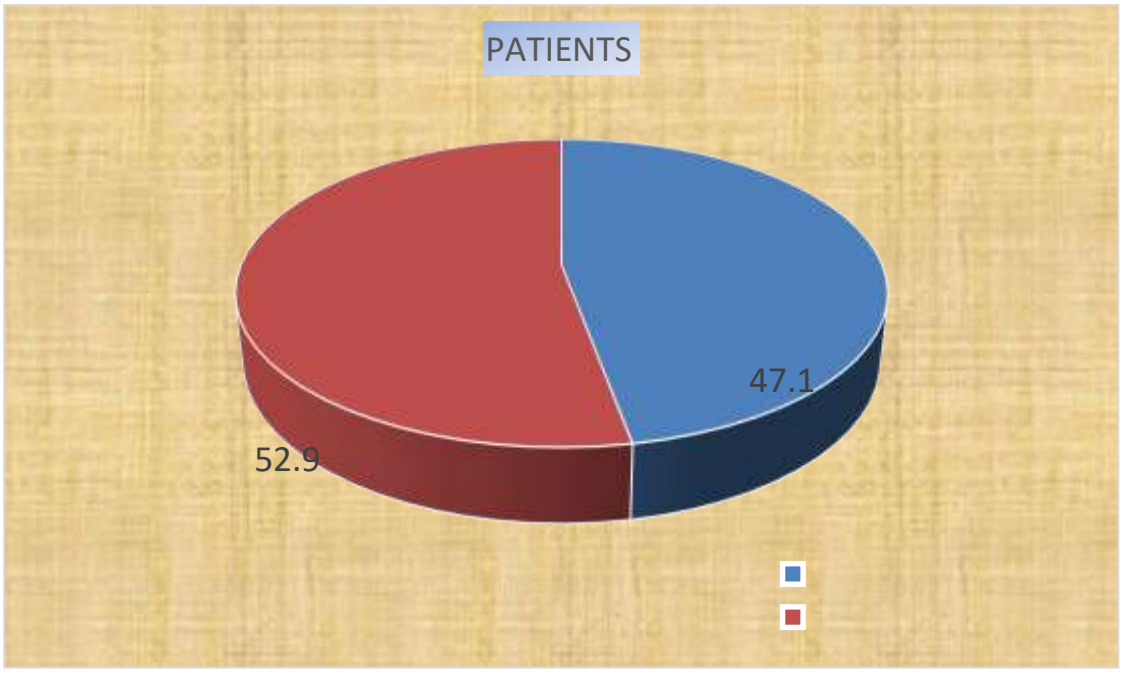


Fig 8 : FNAC smear study with Reactive hyperplasia of lymph node.

RESULTS

Table 1 : Distribution of patients in hospital

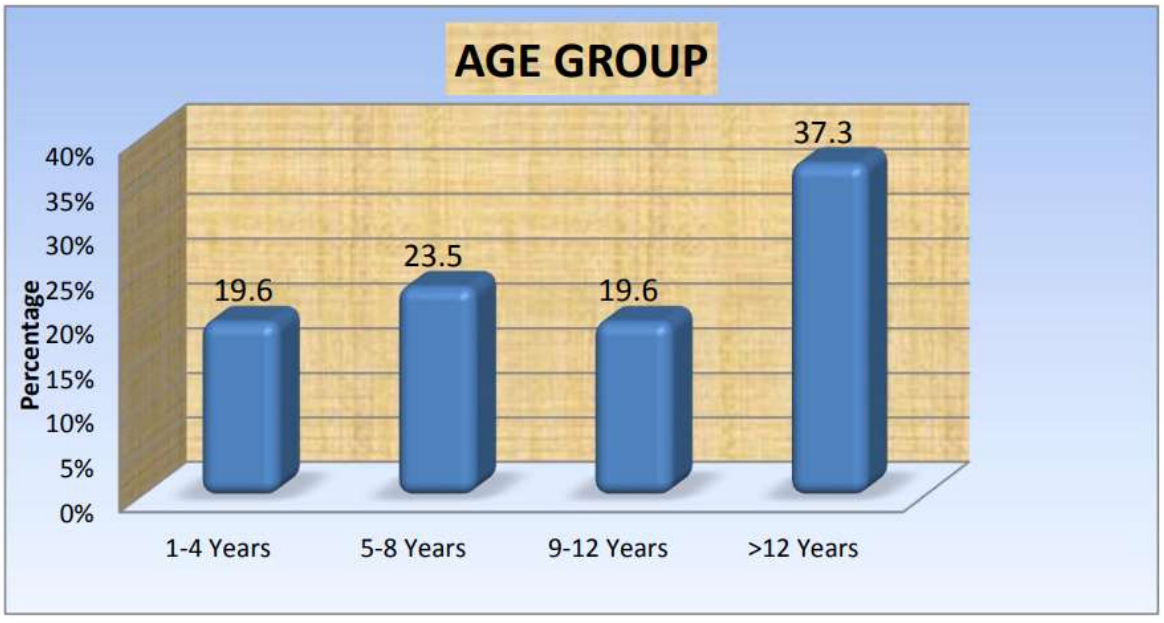
		Frequency	Percent
Patients input	Inpatients	24	47.1
	Out patients	27	52.9
	Total	51	100.0



A total of 51 cases were studied in a period of 18 months starting from November 2014 to May 2016. Out of them 24 (47.1%) were inpatients and 27(52.9%) were outpatients visiting AH and RC.

Table 2 : Age wise distribution of patients

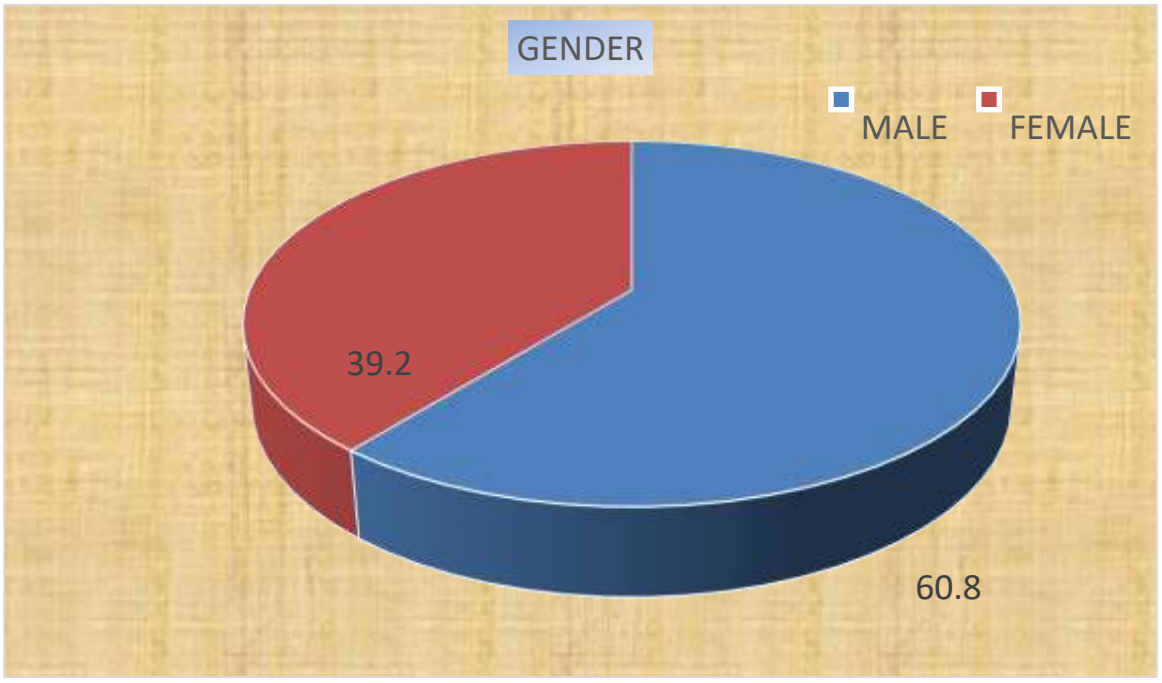
In years		Frequency	Percent
Age group	1-4	10	19.6
	5-8	12	23.5
	9-12	10	19.6
	>12	19	37.3
Total		51	100.0



Majority of patients having Lymphadenopathy were in age group 12-18 years 19(37.3%) followed by 5-8 years 12(23.5%) and the least in 1-4 year group .The youngest patient in our study was 6 months of age.

Table 3: Gender wise distribution of patients

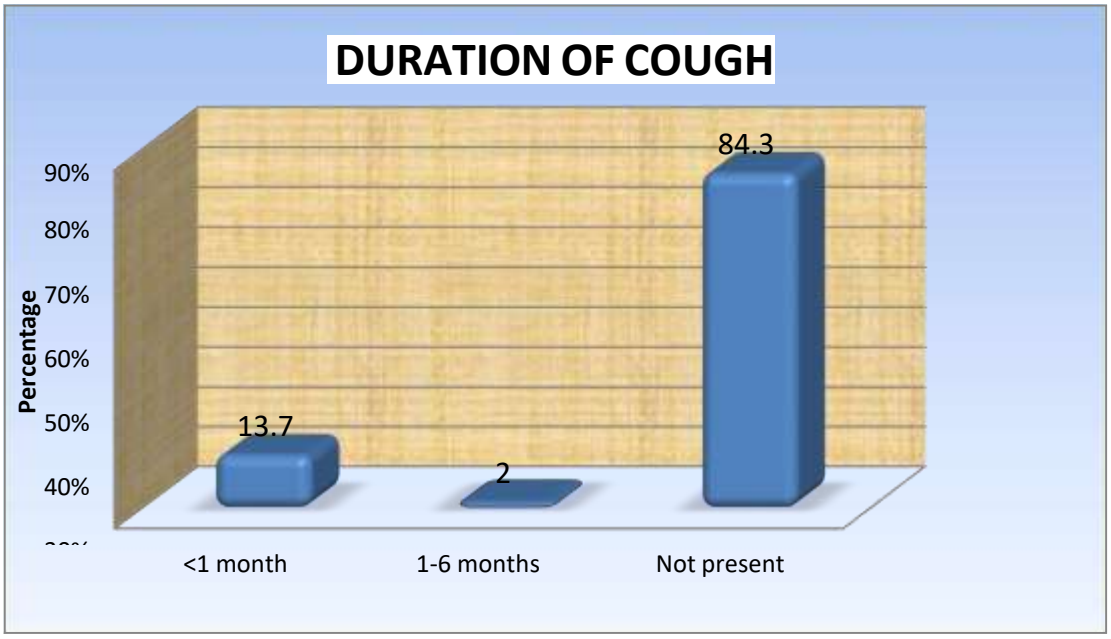
		Frequency	Percent
Gender	Female	20	39.2
	Male	31	60.8
	Total	51	100.0



Significant Lymphadenopathy was found more in males 31(60.8%) comparedto 20(39.2%) in female patients with the ratio being 1.55 : 1.

Table 4 : Distribution of patients with duration of cough

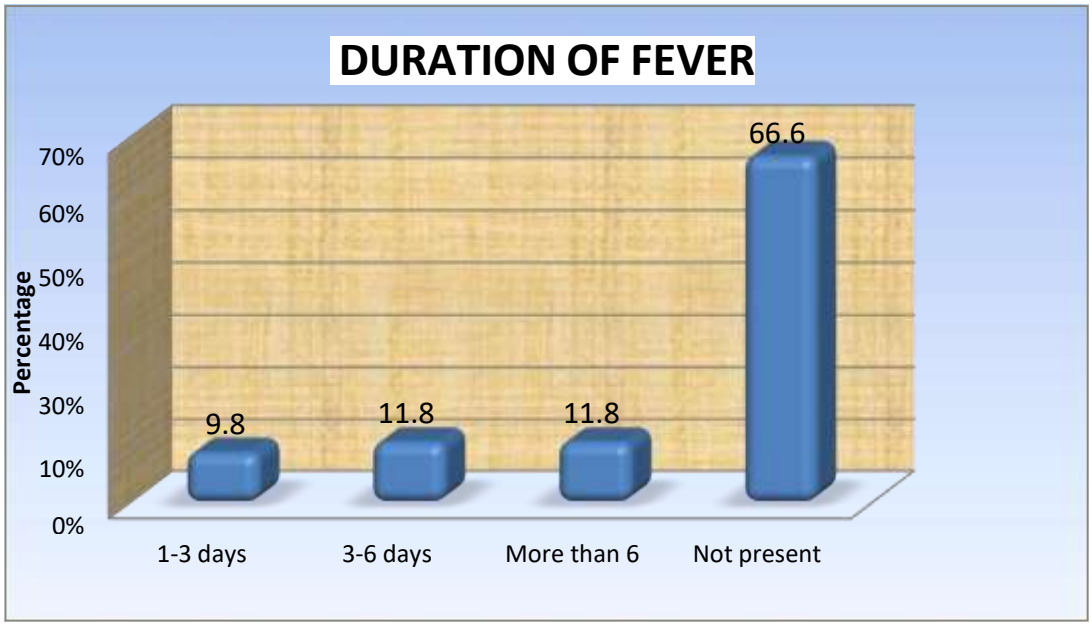
		Frequency	Percent
Duration of cough	<1m	7	13.7
	1-6m	1	2.0
	Not present	43	84.3
	Total	51	100.0



Cough was the presenting symptom in 8 cases (15.6%) out of which 7 (13.6%) cases are having the cough of duration less than 2 weeks while one case was having cough for more than 2 weeks. Majority of the patients didn't have cough as the initial presentation.

Table 5 : Distribution of patients with duration of fever

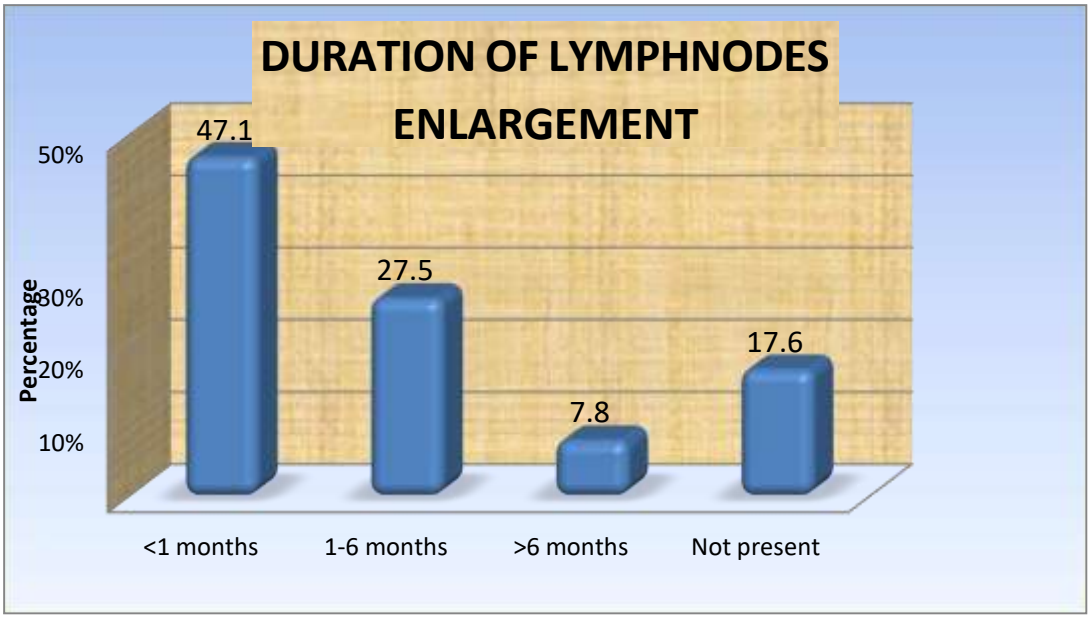
		Frequency	Percent
Duration of fever	1-3 days	5	9.8
	3-6 days	6	11.8
	More than 6 days	6	11.8
	Not present	34	66.6
	Total	51	100.0



17 cases were presented with fever(.33%) 6 of them were having fever for duration 1week (11.8%) or more ,another 6 of them were having fever for duration of3-6 days (11.8%) while 5 of them were having fever for 1-3 days (9.65).

Table 6:Lymph nodes

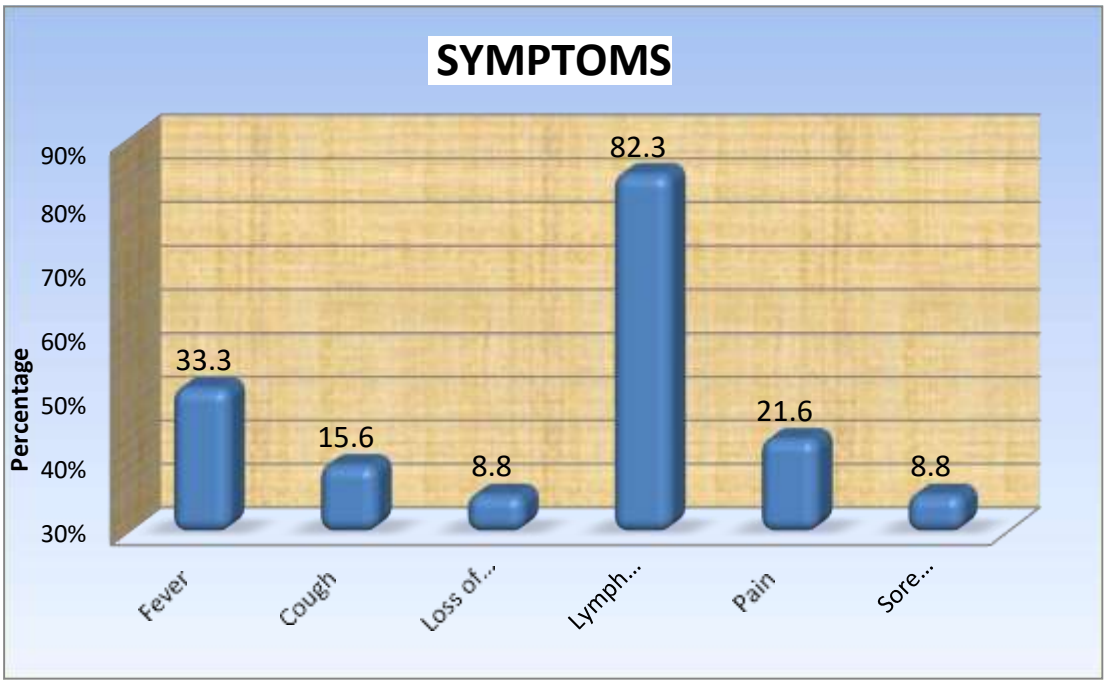
		Frequency	Percent
Duration of lymph node swelling	<1 months	24	47.1
	1-6 months	14	27.5
	>6 months	4	7.8
	Not present	9	17.6
Total		51	100.0



Lymph nodes were noticed in 24 (47.1%) cases within a period of 1 month ,where as 14 cases (27.5%) presented within the duration of 1-6 months ,and few 4 (7.8%) cases presented after 6 months. The nodes were not noticed by the patients andwere found on clinical examination in 9 cases (17.6%).

Table 7 : Symptoms

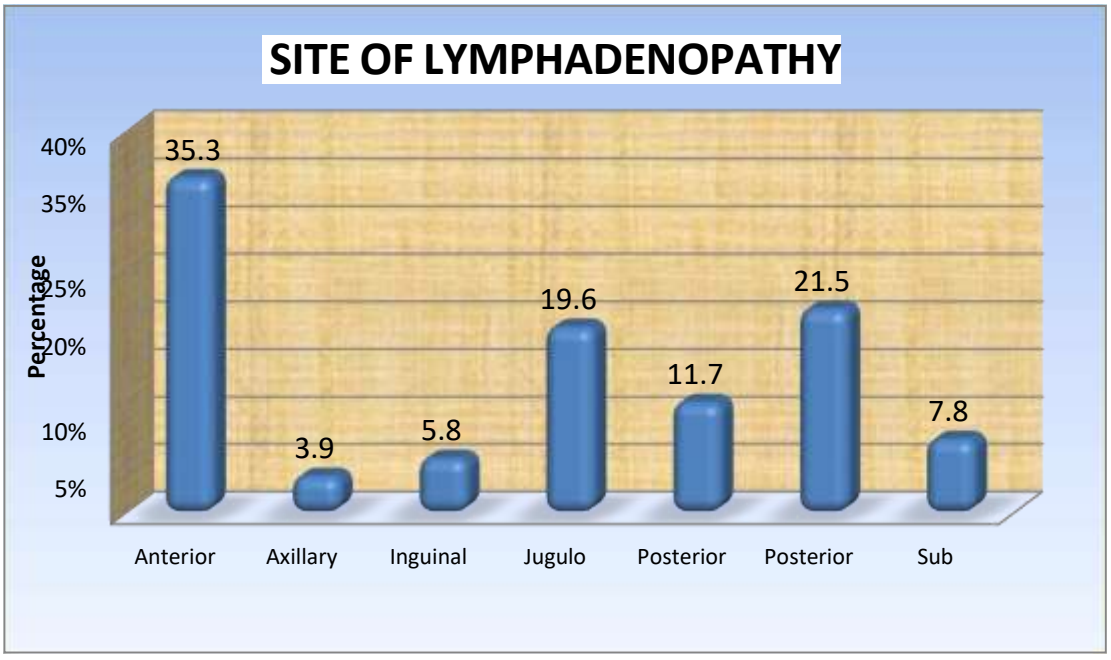
		Frequency	Percentage
Symptoms	Fever	17	33.3
	Cough	8	15.6
	Loss of appittie/weight	3	8.8
	Lymph node noticed	42	82.3
	Pain	11	21.6
	Sore throat	5	8.8



Swelling was the presenting compliant in 42 (82.3%) of the cases while 9 did not notice the swelling. Fever was the presenting compliant in 17(33.3%) while coughwas presenting compliant in only 8 (15.6%) of the cases. Swellings were painless in 40 cases while soar throat was the presenting compliant in 5 cases.History of Ear discharge is present in 1 case(1.96%).

Table 8:Sites of lymphadenopathy .

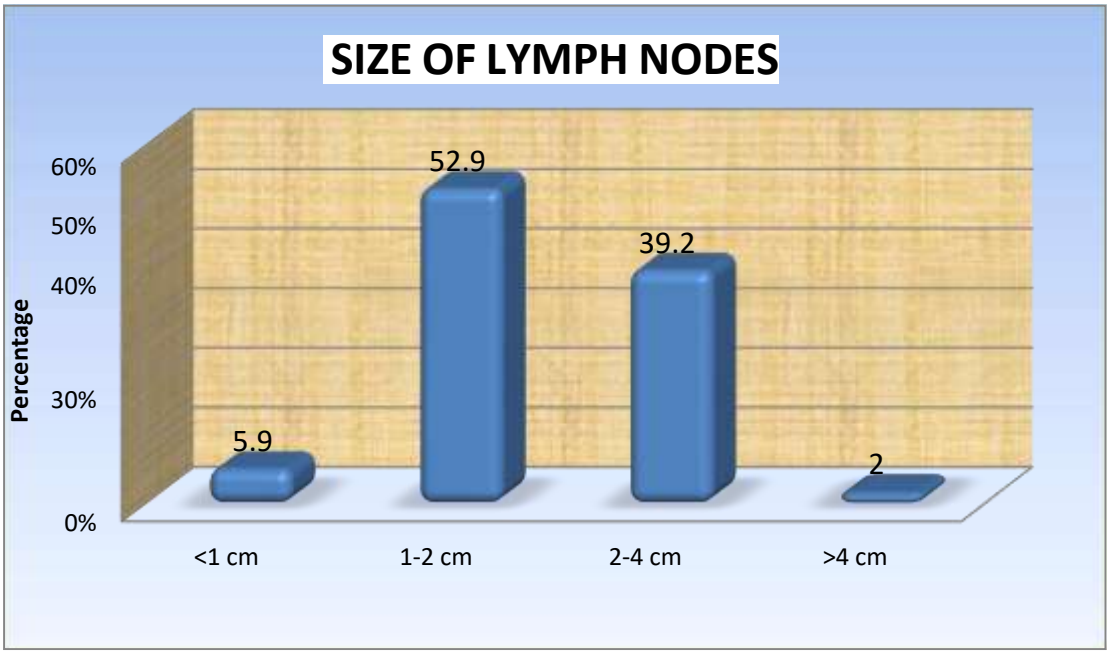
		Frequency	Percent
Sites of lymph nodes	Anterior cervical	18	35.3
	Axillary	2	3.9
	Inguinal	3	5.8
	Jugulo Digastric	10	19.6
	Posterior Auricular	6	11.7
	Posterior cervical	11	21.5
	Sub Mandibular	4	7.8



Anterior cervical region was the most frequent area of finding significantlymph nodes 18 (35.3%) followed by posterior cervical (21.5%) and Jugulo digastric10. (19.6%). 6 cases were seen in Posterior auricular (11.7%) , 3 in inguinal(5.8%) and 2 in axillary region.(3.9%)

Table 9: Size of lymph nodes

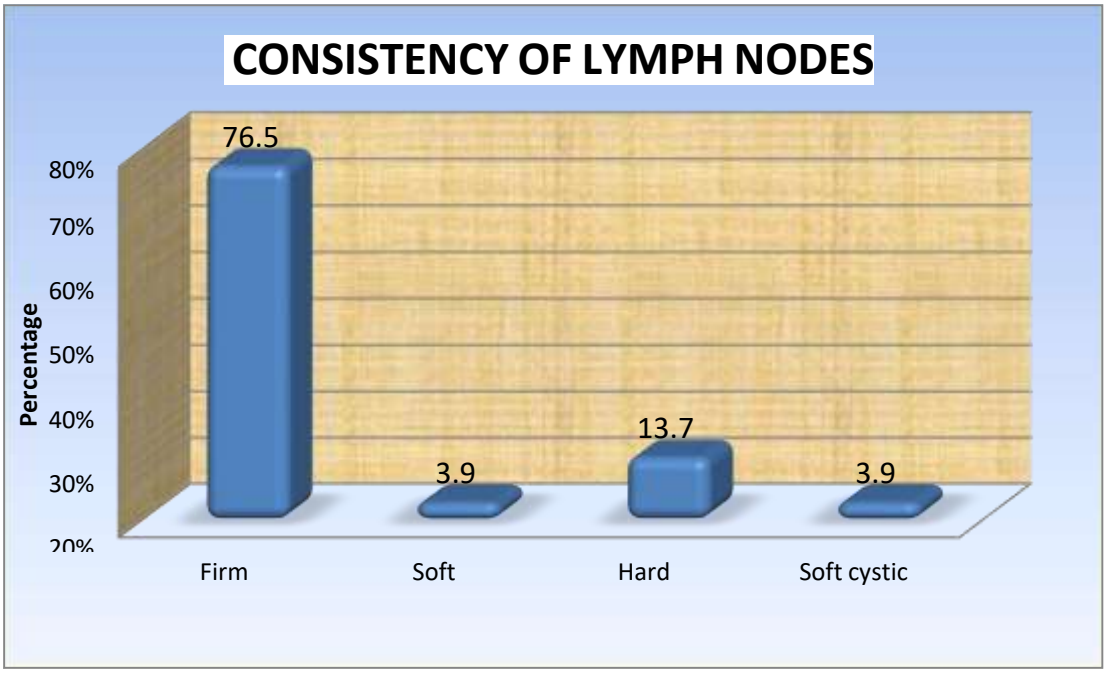
		Frequency	Percent
Size of lymph nodes	<1 cm	3	5.9
	1-2 cm	27	52.9
	2-4 cm	20	39.2
	>4 cm	1	2.0
	Total	51	100.0



Majority of the significant lymph nodes were in the size range of 1-2 cm27(52.9%) followed by 2-4 cm20 (39.2%) .3 (5.9%)cases were <1 cm which were mattedand only 1 case with size > 4 cm

Table 10 : Consistency

		Frequency	Percent
Consistency	Firm	39	76.5
	Soft	2	3.9
	Hard	7	13.7
	Soft cystic	2	3.9
	Soft to firm	1	2.0
	Total	51	100.0



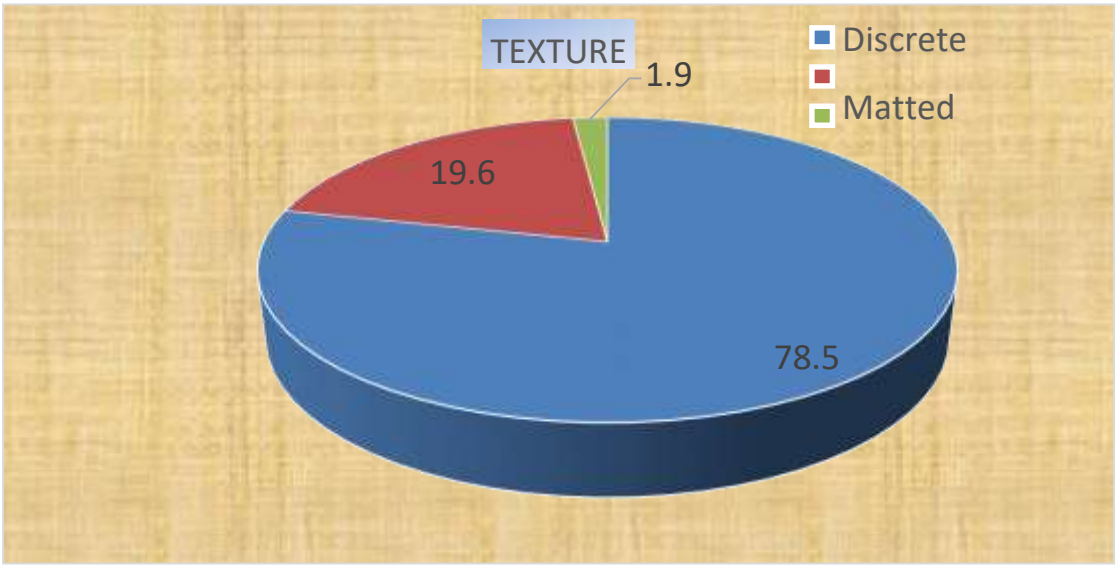
Majority of significant lymph nodes were of firm in consistency 39(76.5%) followed by soft in consistency in 7 (13.7%) ,soft cystic in 2 (3.9%) hard in 2 cases (3.9%) a nd soft-firm in 1 (2%) case

Table 11 : Mobility

		Frequency	Percent
	Mobile	51	100.0

Table 12: Matted/Discrete/Sinus Discharge

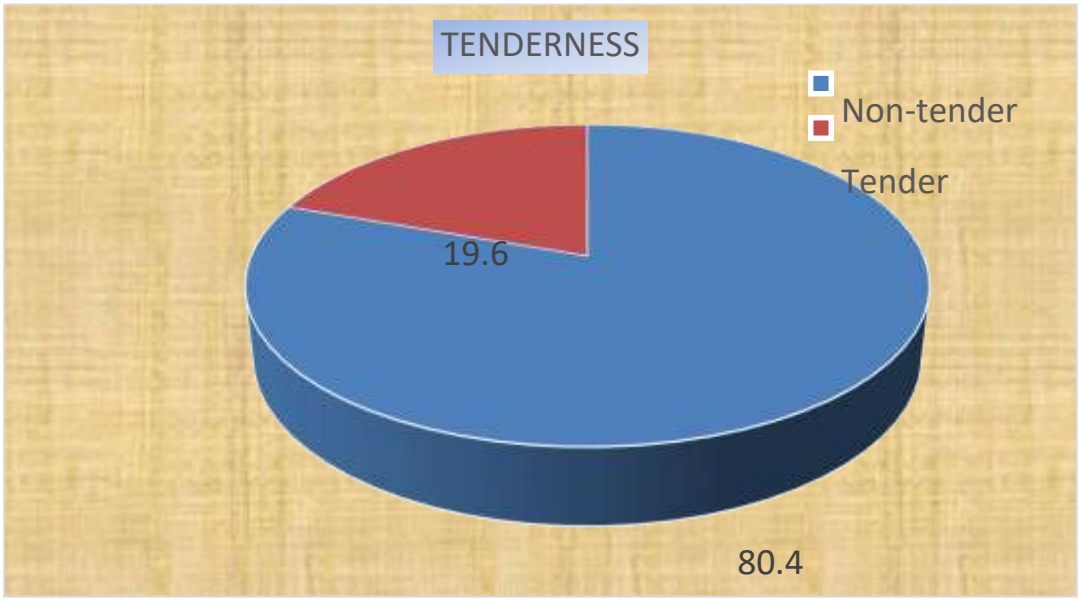
		Frequency	Percent
	Discrete	40	78.5
	Matted	10	19.6
	Sinus Discharge	1	1.96
	Total	51	100.0



Most of the lymphnodes were discrete accounting to 40(78.4%) of all examined while matted nodes accounted to 10 (19.6%) of the lymph nodes.Sinus discharge was observed in only 1 case accounting to 1.96%.

Table 13 : Tenderness

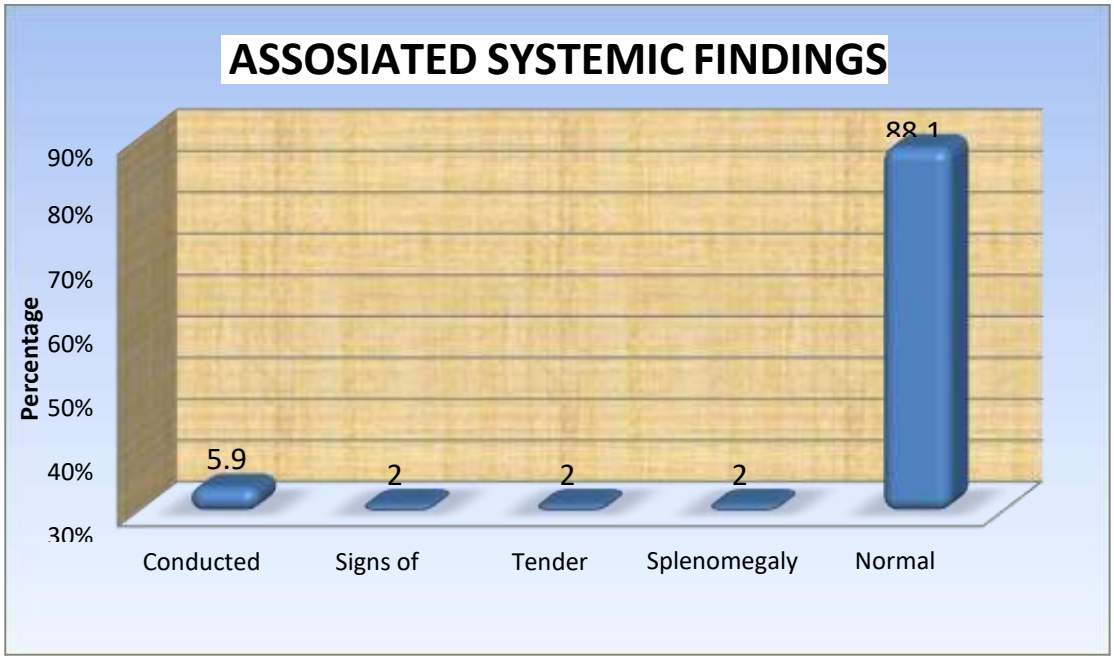
		Frequency	Percent
Tenderness	**Non-tender**	41	80.4
	Tender	10	19.6
	Total	51	100.0



Tenderness was associated with lymphadenopathy in 10 cases (19.6%),rest ofthem 41 were non tender.(80.4%)

Table 14: Associated Systemic Findings:

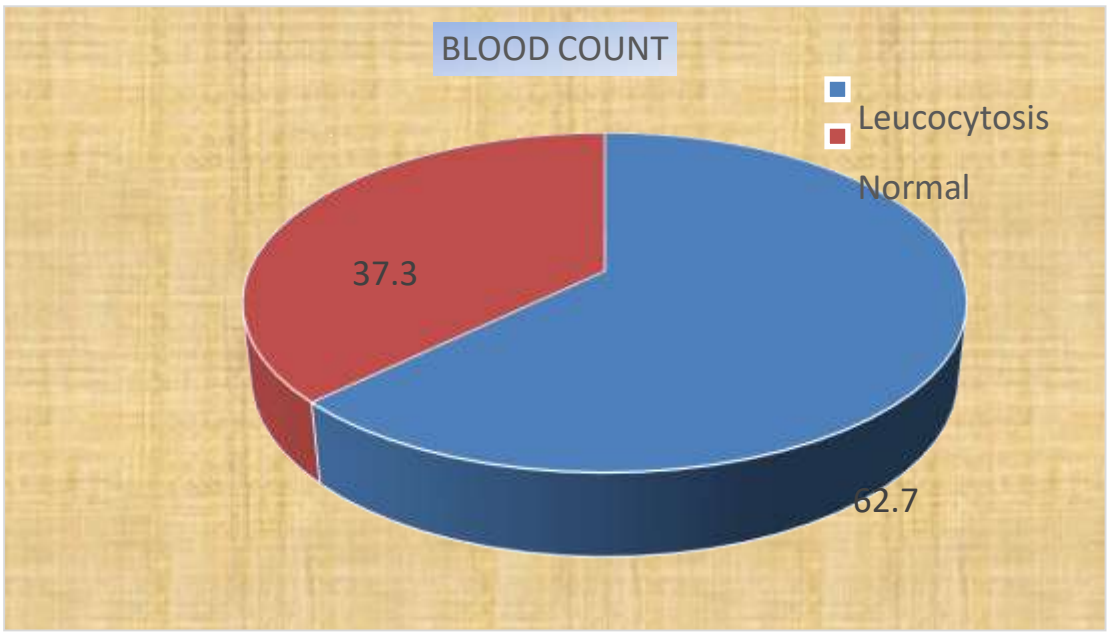
		Frequency	Percent
Valid	Conducted Sounds, Crepitations in Lung Auscultation	3	5.9
	Tender Abdomen	1	2
	Signs of meningitis	1	2
	Splenomegaly	1	2.0
	Normal	45	88.1
	Total	51	100.0



Systemic examination revealed Conducted sounds /crepitations in 3 cases, (5.9%) splenomegaly and tender abdomen in 1 of each cases (2%) and signs of meningitis in 1 case. In 45 cases (88.1%), Systemic examination was found to be normal.

Table 15 :Blood Counts

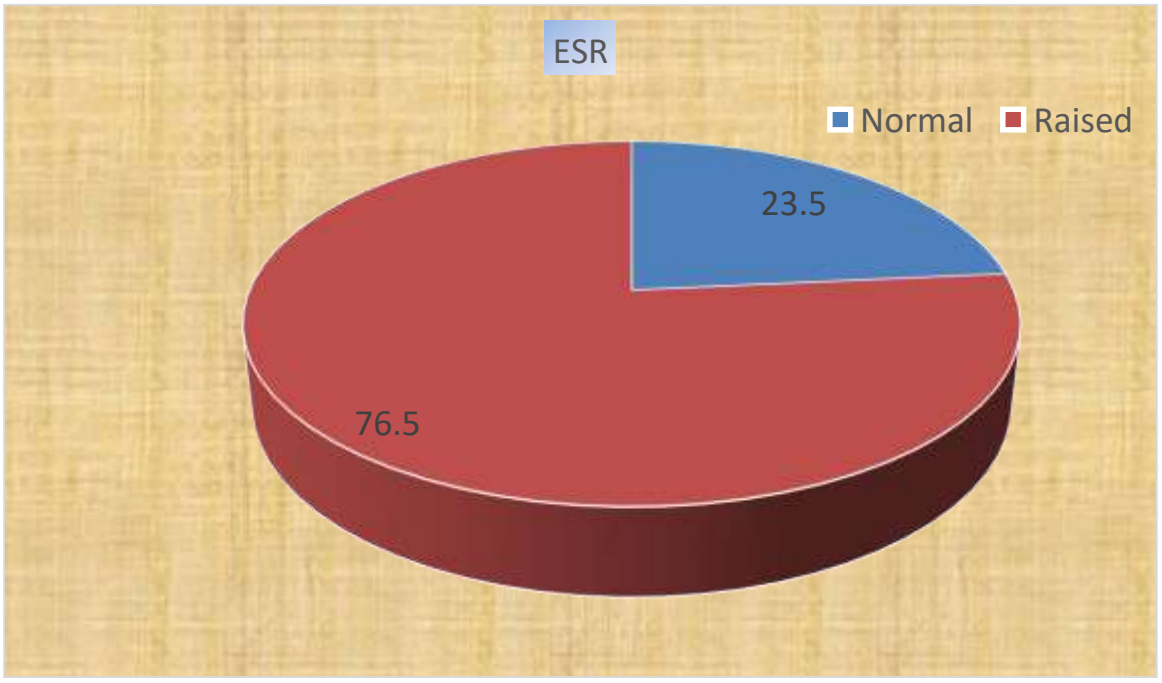
		Frequency	Percent
DLC	Leucocytosis	32	62.7
	Normal	19	37.3
	Total	51	100.0



Leucocytosis was found in 32 (62%) cases. In rest of the cases WBC counts werefound to be within the normal range.

Table 16 : ESR

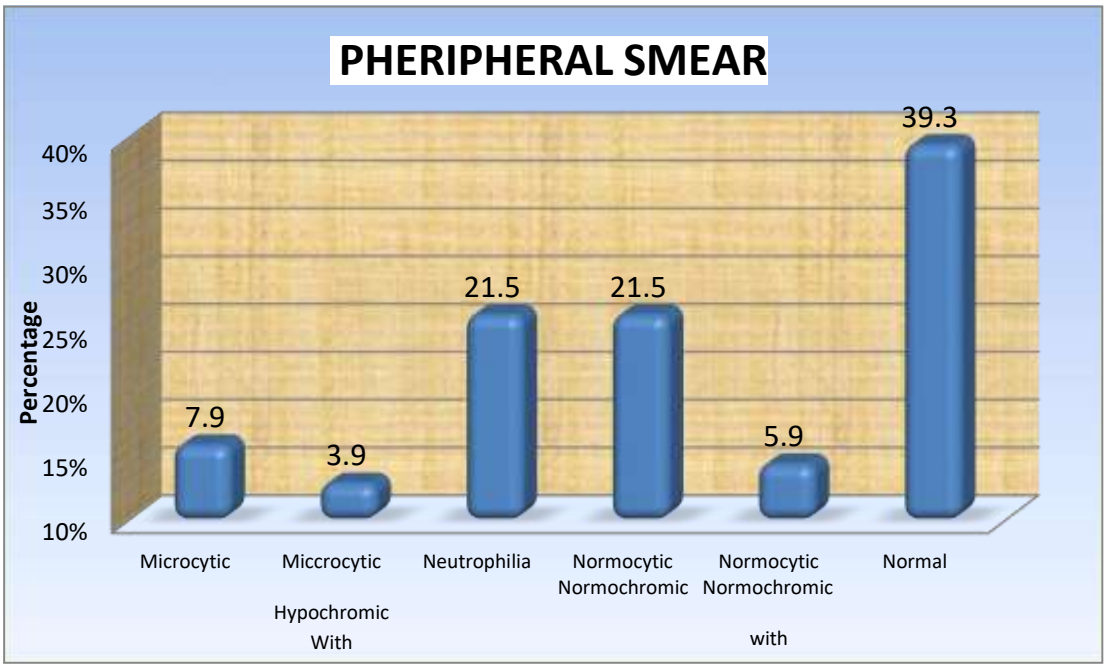
		Frequency	Percent
ESR	Normal	12	23.5
	Raised	39	76.5
	Total	51	100.0



ESR was raised in 39 cases (76.5%) ,and remained normal in rest of the 12(23.5%) cases.

Table 17: Peripheral smear

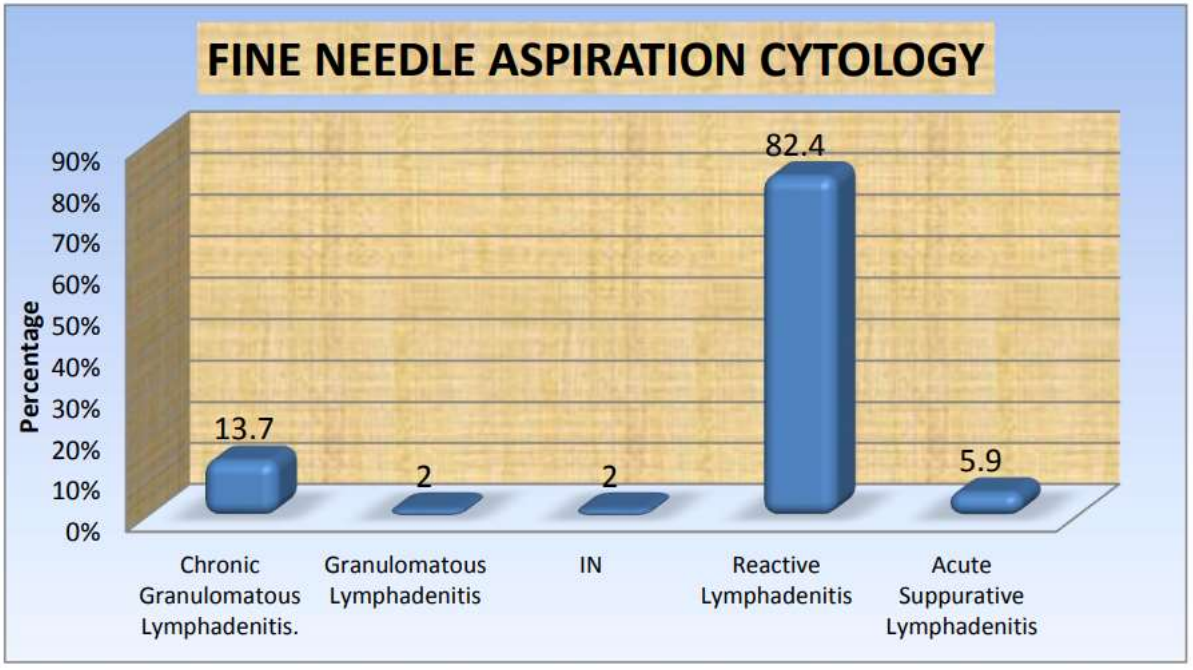
		Frequency	Percent
PHERIPHERAL SMEAR	Microcytic Hypochromic	4	7.9
	Miccrocytic Hypochromic With Lymphocytosis	2	3.9
	Neutrophilia	11	21.5
	Normocytic Normochromic.	11	21.5
	Normocytic Normochromic with esinophillia	3	5.9
	Normal	20	39.3
	Total	51	100.0



Nutrophilia was found in 10 (19.5%) cases Lymphocytosis is observed in 4 cases(78.4%) , where as anemia is found in - and 6 cases had Microcytic Hypochromic anemia (11.7%)

Table 18: Fine needle aspiration cytology

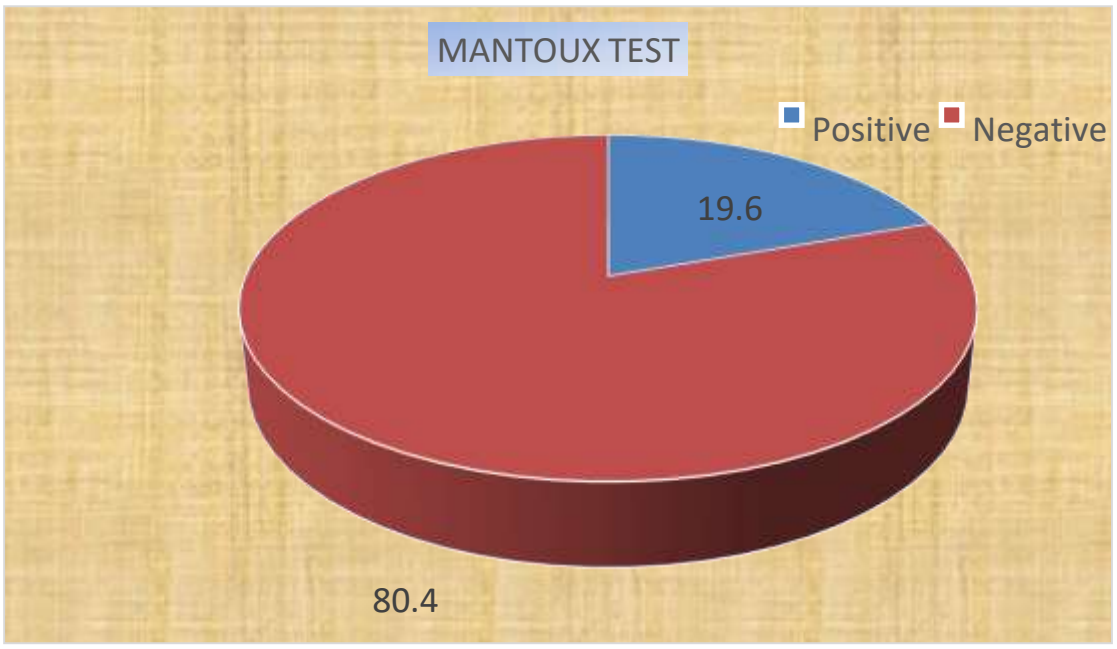
		Frequency	Percent
Fine needle aspiration cytology	Caseating Granulomatous Lymphadenitis.	7	13.7
	Granulomatous Lymphadenitis	1	2.0
	Insignisicant	1	2.0
	Reactive Lymphadenitis	39	82.4
	Acute Suppurative Lymphadenitis	3	5.9
	Total	51	100.0



Reactive Hyperplasia was found in the FNAC studies in 37 (72.5%) cases followed by Caseating Granulomatous findings in 7 (13.7%) of the cases, FNAC suggestive of Suppurative lymohadenitis in 4(7.4%) , Granulomatous lymphadenitis, Benign Fibrous Histiocytoma were found in one cases each. The sample obtained is insufficient to comment in one case.

Table 19:Mantoux test

		Frequency	Percent
Mantoux test	Positive	10	19.6
	Negative	41	80.4
	Total	51	100.0



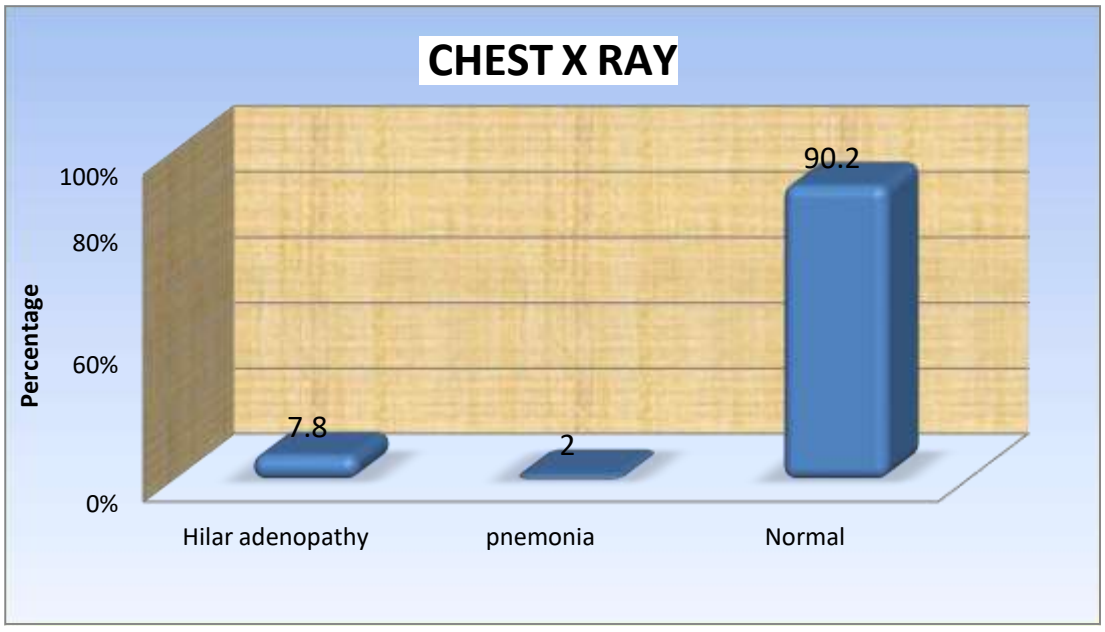
Mantoux test is positive in 10 cases (19.6%) and all of them were showing chronic lymphadenitis and were diagnosed as Tuberculosis with other clinical findings and investigations

AFB is positive in 2 cases accounting to 3.9% of the cases.

Staphylococcus. was present in cultures of aspirate or lesions in 6(11.76%) cases while 5 (8.1%) cases had Streptococcus in culture growth and one (1.96%) had Pseudomonas aeruginosa.

Table 20 : Chest X ray

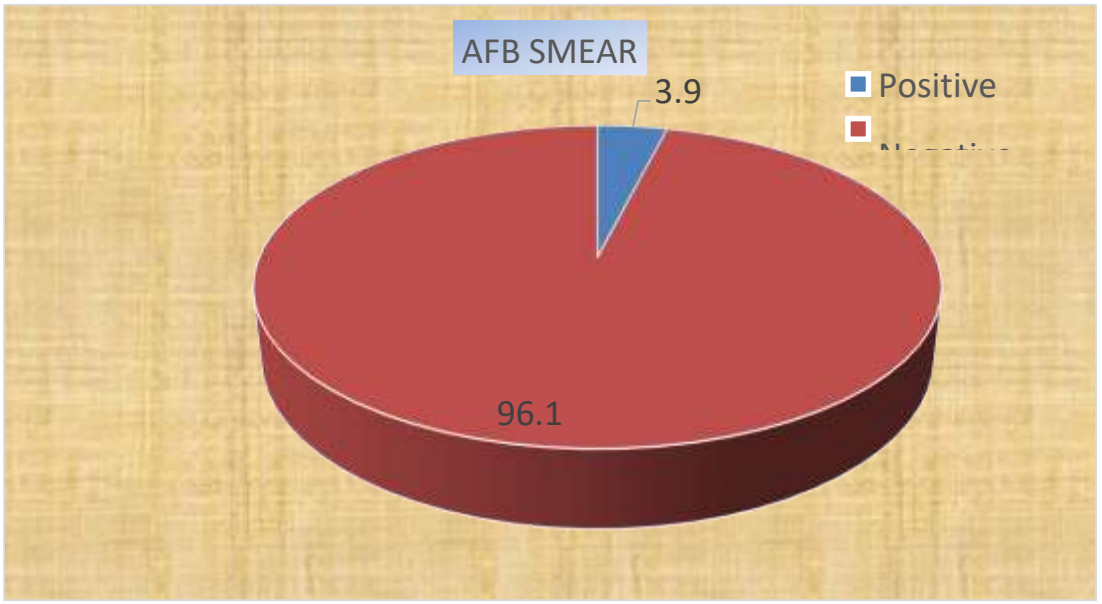
		Frequency	Percent
CHEST X RAY	Hilar adenopathy	4	7.8
	Pneumonia	1	2.0
	Normal	46	90.2
	Total	51	100.0



Chest Roentgenogram was showing Hilar adenopathy in 4 (7.8%) of the cases followed by Pneumonic consolidation in 3(5.8%). ,where as both the findings were seen in 2 cases (3.9%).Chest X-Ray showed normal study in 46 cases(90.1%).

Table 21 : AFB stating

		Frequency	Percent
AFB	Negative	49	96.1
	Positive	2	3.9
	Total	51	100.0



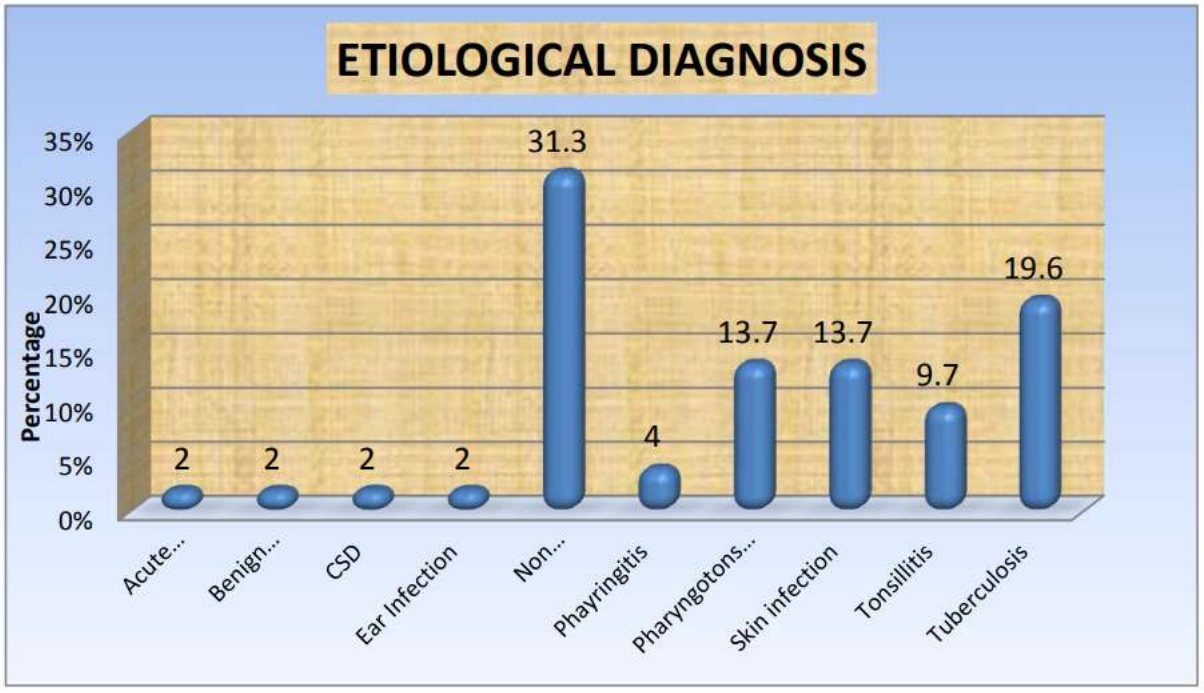
AFB was positive in samples of only 2 cases (3.9%).

Table 22: Treatment

		Frequency	Percent
Treatment	AB	26	51.0
	AB,AI	1	2.0
	AB,SX	1	2.0
	AI	10	19.6
	ATT	10	19.6
	SX,AB,AI	3	5.9
	Total	51	100.0

Table 23: Etiological Diagnosis:

		Frequency	Percent
Differentia; Diagnosis	Acute appendicitis	1	2.0
	Benign FibrousHistiocytoma	1	2.0
	CSD	1	2.0
	Ear Infection	1	2.0
	Non diagnostic hyperplasia	16	31.3
	Pharyngitis	2	4.0
	Pharyngo tonsilitis	7	13.7
	Skin infection	7	13.7
	Tonsillitis	5	9.7
	Tuberculosis	10	19.6
	Total	51	100.0



Final diagnosis in a case of Significant Lymphadenopathy was made in 35 cases while the remaining 16(31.3%) were considered as Non Diagnostic Hyperplasia.Local infections like Pharyngitis2(4%,) tonsillitis 5(9.7%)(,Pharyngotonsillitis7(13.7%), skin infections7 (13.7%) were found in most of the cases .Tuberculosis was diagnosed in 10 (19.6%)cases, where as one (2%) of the each case were diagnosed as CSOM, CSD, Acute appendicitis, Benign Fibrous Histiocytoma.

Table 24: Area wise distribution of lymph nodes VS etiology

		Tuberculosis	**Local infection**	**Non diagnostic Hyperplasia**
Sites of lymph nodes	Anterior cervical	4	6	8
	Axillary	0	2	0
	Inguinal	0	0	2
	Jugulo Digastric	0	7	1
	Posterior Auricular	1	3	2
	Posterior cervical	3	3	3
	Sub Mandibular	0	2	0
	Generalized lympahdenopathy	1	1	1

Majority of local infections (6 cases) had Jugulodigastric lymph node enlargement. In Tuberculosis group of patients 4 were having Anterior cervical lymphnodes and 3 were having posterior cervical lymph node enlargement while 1 case had posterior auricular enlargement.8 cases of NDH had anterior cervical nodes,3 were having posterior cervical lymph node enlargement while 2 had posterior auricular and inguinal and 1 had JD nodes enlargement.

Table 25: ESR, Chest X Ray, Mantoux test, FNAC in Tubercular Lymphadenitiscases.

Test	Number of cases	Percentage
Chest x ray(suggestive features)	5	50
Mantoux test	10	100
FNAC	7	70
Raised ESR	10	100

Chest X Ray was suggestive in 5 cases (50%) of Tuberculosis. FNAC was suggestive of Tuberculosis in 7(70%) of the cases. Mantoux test and raised ESR were found in all (100%) the cases of Tuberculosis.

Table 26: ESR VS Etiology:

	Tuberculosis	Local infection	NDH	Others
Raised ESR	10	17	10	2

ESR is raised in all cases of TB, where as only 27(65.8%) in the remaining cases.

Table 27: Blood counts VS Etiology:

Blood count	Tuberculosis(n=10)	Local infetions	NDH
Leucoytosis	7	-	16
Lymphcytosis	3	1	0
Neutrophilia	2	8	1
Esinophilia	-	3	-

Lymphocytosis VS TB:

Lymphocytosis was observed in 3 cases out of 10 TB cases while it was observed in one case of remaining non TB cases which is statistically significant,(p=0.0004)

Nutrophilia VS Local infection group:

Nutrophilia was found in 8 of 23 cases having local infections where aswithout a local infection group had only 2 cases of nutrophilia which is statistically significant.(p=0.013)

Microcytic Hypochromic anemia VS Tuberculosis:

MHA was observed in 5 out of 10 cases of TB where as observed in only 1 of the remaining 41 cases (p=0.0001) which was statistically significant.

DISCUSSION

The present study was intended to study the etiological and pathological profile of significant pediatric lymphadenopathy after correlating the history, clinical examination , laboratory reports as well as the aspiration cytology.

In total 51 children between 6 months to 18 years with significant lymphadenopathy consulting the Department of Pediatrics, Adichunchanagiri Hospital & Research centre, BG Nagara were studied.

It was found that majority of the patients with significant lymphadenopathy were in the age group of above 12 years (37.3%) followed by 5- 8 years (23.5%) ,1-4 years (19.6%) . Mishra SD et al in their study observed 36.5% patients in 4-8 yrs age group and 24.1% in 8-12 years age group[35] Normal peak lymphatic growth occurs in the age group of 4-8 yrs, nearly reaching pathological size. So with on-going antigenic stimulus the lymphoid growth may exceed the normal limits. Though Knight PJ et al emphasized that age is not important in predicting the incidence of significant lymphadenopathy [23.]

In our study incidence in males was more compared to females with male to female ratio 1.55:1. Moore et al found male preponderance with male to female ratio 3:1. Mishra SD et al observed slightly higher incidence in males with male to female ratio 1.1: 1[35] sheikh MP et al observed higher incidence in males (55.6%) as compared to females(44.4%) [21] .This may be explained by the customary provision of additional care to male children compared to female child but as such there was no biological susceptibility.

In majority of patients the presenting symptom was swelling in the region of neck (82.3%) followed by fever (33.3%) and cough (15.6%). This was similar to the study by Reddy MP et al who studied 100 children with generalized lymphadenopathy observed neck swellings as the most common presenting symptom(52 %of cases)[28.] Sheikh MM et al observed history of swelling in 100% of cases, andfever in 86 % of the cases. But the above study considered only the cases with tubercular lymphadenitis. This highlights the importance of thorough clinical examination in finding significant lymph nodes in addition to history taking in diagnosis of lymphadenopathy as 17.7% of cases did not present with the swelling as chief compliant.

Duration of the lymph node swelling was less than one month in 47.1% , morethan 1 month and less than 6 months in 27.1% of the cases, and more than 6 months in 7.8%% of the cases. Sheikh MM et al observed the duration of enlarged lymph nodes to be l month to 6 months in 51%, more than 6 months in 25% cases and less than 1 month in 8% of the cases[21].

In our study, Anterior cervical nodes were commonly involved in (35.3%) of cases. Knight PJ et al observed in their study of 239 children with lymphadenopathy, 47% of children having upper anterior cervical lymph node enlargement which formed predominant site of cervical lymphadenopathy[23].

Majority (76.5%) of the enlarged nodes were firm in consistency in the presentstudy which is similar to the study by Lake & Oski et al who observed firm nodes in all 45 cases with cervical lymph node enlargement[22].

In the present study matted lymph nodes were found in 19.6% of the cases. In majority (78.5%) of the cases the nodes were discrete and mobile. One case had discharging sinus. This was similar to the study by Mishra SD et al, who observed thematted nodes in 6-10% of their patients.[35]

In majority (80.4%) of the cases in present study the enlarged nodes were non- tender.

In the present study discharging sinus formation was observed in 1 case (2 %) Mishra SD et al in their study of cervical lymphadenopathy in children found discharging sinus in 1.5% of the cases[35].

In the present study, on clinical examination 27.5% cases had Tonsillitis and / or Pharyngitis; ear infection like Otitis media was found in 1.96 % of cases; 13.7 % had skin lesions over scalp like impetigo . Among 20 cases of bilateral lymphadenopathy, 55% had pharyngitis / tonsillitis in etiology.

Systemic examination revealed organomegaly (Hepatomegaly and / or splenomegaly) in 1.96 % of the cases.

Barton LL et al in their study observed that out of 74 children with cervical lymphadenopathy 49% had pharyngitis and or tonsillitis, 32% had impetigo, 16% had otitis media, 7% had splenomegaly and 5% had hepatomegaly[33].

In the present study the commonest organisms isolated were staphylococcus and streptococcus in each 9.2% of the cases. Dajani s et al found streptococci to be thecommon organism isolated in their study of 34 cases of cervical lymphadenitis in children[32]. Reddy MP et al did 30 throat swab cultures out of which 50% were culturepositive[28]. Staphylococci were isolated in 2 and streptococci in 23.3% of their cases. Chylak J studied bacterial throat flora in acute successive pharyngitis and tonsillitis in children and found that staphylococcus aureus was isolated most commonly followed by H. influenza and Beta hemolytic streptococci [65]

Thus in the above studies and in the present study the most common organisms isolated in tonsillitis/pharyngitis cases were streptococci and staphylococci.

5 cases (9.2 %) of the children in the present study had soft , fluctuant with overlying erythema and needed incision and drainage. Culture of the aspirates of 3 cases (60%) from these nodes grew staphylococcus aureus, and in others cultureswere not done as they were already on antibiotics

Ear swab cultures in the present study grew pseudomonas in the only case. Ojala KS et al isolated staphylococcus aureus in 22% pseudomonas in 19%, and proteus in 5% of cases in chronic suppurative otitis media[66].

Constable and Butler isolated staphylococcus aureus in 29%, proteus in 26 andPseudomonas in 15% out of 7 cases with scalp lesion 2 (28.6%) cultures of staphylococcus aureus were isolated, indicating that staphylococci to be the common organisms responsible for pyoderma or impetiginous lesions[67].

Raised ESR in the present study was found in 76.5% of the patients with rate 21.13 mm /hr as mean sedimentation and a range of 1.0-60 mm/hr .The observation by Barton LL et al with mean sedimentation rate of 38mm / hr range 3.0-59.0 was more compared to our study[33].

Anemia was present in 41% of the children in the present study. It correlates with the present national incidence of anemia in pediatric population[72].

Leucocytosis was observed in 62.7 % of patients in the present study with mean 13210/ cu mm, range 4500-22000. In a study by Barton LL et al mean leukocyte count was 13300 / cu mm range 3600-32100[33].

Lymphocytosis was observed in 7.8 % of patients in the present study of which 75% had tuberculosis as etiology which is statistically significant. P=0.0004.

Bedside FNAC was done in all the cases as a primary diagnostic tool in the evaluation of children with cervical lymphadenopathy. In the present study cytological material is sufficient to report in 50 (95.7%) out of 51 cases. In 1 case (2%) the material was inadequate for giving any opinion .This was similar to the observation by Sarda AK et al who reported adequate aspirate of 97.5% in their study groups[38].

No complications in any form were noted in present study Sarda AK et al reported no complications after FNAC in their study.

In majority of the cases in present study cytological picture was of reactive hyperplasia 82.4% followed by granulomatous lesion in 15.3% and pus was aspirated (suppurative) in 3 cases (5.9%).

Mishra SD et al observed reactive hyperplasia in 71.5%, granulomatous changes in 17.5% and abscess in 6.6% and malignancy in 3.6% of their cases[35]. Knight PJ et al in their study of 175 children with cervical lymphadenopathy found reactive hyperplasia in 57.5%, granulomatous changes in 28.2%, and malignancy in 17.9% cases of FNAC[23]. In most of the studies including the present study the predominant cytological finding was that of reactive hyperplasia.

Mantoux test was done in all the cases .Positive reaction was observed in 10 cases (19.6%) in the present study. All the 10 cases had tuberculous etiology with 100% sensitivity highlighting its importance in diagnosing pediatric tuberculosis.

Chest x-ray findings were abnormal in 5 (9.8%) of the cases which are suggestive of tuberculosis. Hilar adenopathy constitutes 8.0% of the abnormal chest X ray finding. 50% of the tuberculosis cases had suggestive radiological findings.

Sheikh MM et al reported abnormal x-ray findings in 44% of their cases[21] but in this series only children with tubercular lymphadenitis were included and all children were having cervical lymphadenopathy.

In the present study we could do serological for HIV only as there was non- availability of other tests like serology for EBV, CMV, and Toxoplasmosis. No case is associated with HIV infection including tuberculosis group in the study.

After correlating history, findings and laboratory tests a specific cause for lymphadenopathy could be identified in 68.7% of the cases. In 48.6% cases it was dueto local infections, 19.6% were due to tuberculosis.

Etiology could not be found in 31.3% of the cases even after hematological, microbiological and radiological investigations and, were considered as non- diagnostic reactive hyperplasia.

For comparison purpose the cases can be divided into acute and chroniclymphadenopathy depending on the duration of lymph node swelling. In 52.9% patients, duration of adenopathy was < 1 month and in 31.3%patients the duration was > 1 month. 8 cases (15.6%) did not notice the swelling at all.

The etiologies in patients with acute lymphadenopathy were tonsillitis and / or pharyngitis in 27.4%. Ear infection in 1 .96 %, skin infection in 13.7%.

Most commonly isolated organism from the source of infection wasstreptococci in 9.8%, staphylococci in 9.8%, pseudomonas in 1.96 % cases. In 3.92 % cases no pathologic organism was isolated.

Barton LL et al studied 74 cases of cervical lymphadenitis in children and in 93% of cases duration was 1 month. They performed cultures from local source of infection (throat, scalp, ear and also lymph node aspirates) and found that staphylococcus was responsible for 36.4% of cases, streptococci for 26%. and pseudomonas in 1.3%. In 24% cases cultures were negative[33].

Wright JE et al did retrospective study of 78 children with acute cervical lymphadenitis over nine years. The commonest organism isolated was staphylococcusCommon organism in the present study was streptococci in 33.3%. In 31 patients, the duration of lymph node swelling was 1 month[69]. Chronic lymphadenopathy significantly associated with these serious systemic diseases ($p < 0.05$).

Moore SW et al studied surgically excised cervical lymph nodes from 1332 children aged less than 15 years, with chronic lymphadenopathy in a developing country in Africa[36]. Tubercular lymphadenitis was seen in 25% of cases, malignanciesin 11.6%, HIV infection in 5(0.4%) cases and in 47,8% cases non specific reactive lymphoid hyperplasia. Other causes found were syphilis. Toxoplasmosis and Histiocytosis. When compared to this study tuberculosis cases were more in our study. This could be due to high tuberculosis infection in this region. We did notcome across any malignancy case.

In a study conducted by Connolly & Mackenzie 93 biopsies of cervical lymph nodes revealed reactive hyperplasia in 64.5% granulomatous lesion in 22,6% and malignancy in 12.5 % of cases .[37]

In present study there was no case with lymphadenopathy due to HIV infection when compared to other studies. This could be due to less number of HIV cases in this region and effective implementation of PPTCT.

Thus, it is evident from the above studies and also in the present study that the causes of acute lymphadenopathy differ from that of chronic lymphadenopathy. In acute lymphadenopathy cases local infections are the predominant causes. In chronic lymphadenopathy tuberculosis is the leading specific cause even though non- diagnostic hyperplasia is likely to be more common in children. In a proportion (7.84%) of the cases with chronic lymphadenopathy in the present study, the etiology could not be ascertained even after hematological, radiological cytological and serological investigations. This observation was higher in study by Moore SW et al (47.8%)[36].

Studies involving detection of antigen and antibodies against lesser known viruses, parasites would have decreased the number of undiagnosed cases.

Since this was a time bound study (18 months period) , long-term follow-up could not be done in these cases to give any opinion regarding further investigation and follow- up. Character of lymph nodes was of diagnostic value. Matted nodes werenoted in 10 cases in the present study out of which the diagnosis in all the cases was tuberculosis. Matted nodes always indicated serious systemic disorder. Fixity to the surrounding structures was found in none while sinus formation was seen in 1 patient and it is due to CSD.

Soft, fluctuant nodes were seen in 9 patients, of which 5 (83.3%) were due to acute bacterial adenitis, 2 (22%) due to tuberculosis. In bacterial adenitis cases there was local rise of temperature, redness of the overlying skin and tenderness which was not seen in tuberculosis case.

Knight PJ et al opined that nodes matted together and nodes fixed to the underlying tissues suggest granulomatous inflammation or neoplastic infiltration and also opined that character of lymphadenopathy may be helpful in determining the cause of lymphadenopathy[23].

Presence of hepatomegaly and or splenomegaly was seen in 2 patients in our study. Serious systemic diseases were diagnosed in 1 of them (50%) as tuberculosis.

Thus the history and physical examination features which were commonly associated with, and which indicated presence of serious systemic diseases like tuberculosis, HIV infection, were chronic duration of symptoms like adenopathy, fever or cough; history of weight loss: unusual characteristics of lymph nodes like matting, fixity to surrounding structures, sinus formation and presence of hepatomegaly and / or splenomegaly

Leucocytosis identified in 32(62.7%) patients was not significantly associated with any particular disease and was not directing towards a particular diagnosis.

Neutrophila seen in 11 cases was more common in the local infections group (14.5%) probably indicating response to acute infections.

Lymphocytosis was more commonly observed in tuberculosis group 5 out of 10 of cases with lymphocytosis and was statistically significant (p=0.0004).

Total counts were of no value in differential diagnosis but lymphocytosis was significantly associated with tuberculosis patient.

Sedimentation rates were raised in 24 out of 51 cases in the present study (41%). probably indicating inflammatory response. In all the 10 cases (100%) of tuberculosis there was rise in ESR.

Morland Bruce et al stated that ESR is a very non-specific test and is of limited benefit as it is commonly raised in a wide range of inflammatory, reactive and malignant conditions. Similarly a normal ESR does not necessarily exclude significant pathology [70,]

FNAC was of value in diagnosing 7 cases. Thus the sensitivity of FNAC in diagnosing tuberculosis was 70%. Various studies have reported the sensitivity of FNAC in diagnosing tubercular lymphadenitis as 16.5%, 77% 80.7%, 84.4%, 95%and 100% [38, 41,42.44,.47] .Thus diagnostic accuracy of FNAC tubercular lymphadenitis varied from 16.5% to 100% in various studies.

By using FNAC 7 out of 10 cases of tuberculosis cases were correctly diagnosed and early, on the same day of visit by the patient. The report was available on the same day. Thus in the present study FNAC as primary diagnostic test was of value in diagnosing 70% of tuberculosis cases. In those with benign conditions like reactive hyperplasia to rule out underlying serious systemic disease and reassuranceof parents. In pyogenic cases to obtain material for culture and antibiotic sensitivity thereby directing antibiotic treatment.

SUMMARY

The cross sectional study was done to study the etiological and pathological profile of significant pediatric lymphadenopathy in children from 6 months -18years attending the hospital from Dec 1st 2014 to May 30th 2016. Detailed history was taken including the family history of contact with tuberculosis, socioeconomic status and immunization. The clinical examination was done in each case and detailed examination of each significant lymph node was done. Hematological investigations were done like complete hemogram , ESR ,peripheral smear, FNAC of the lymph nodes, mantoux test ,sputum/gastric aspirate for AFB for all the cases. Chest X ray, culture and sensitivity, and biopsy were done as required.

After entering the information in the pre designed proforma and after applying descriptive statistics it was observed that the occurrence of significant cervical lymphadenopathy was more common in male children and in the children above 12 years of age.

These children commonly presented with painless swelling in the cervical region with associated symptoms like fever, cough, loss or failure to gain weight and sore throat. The 17.7% of them did not notice the swelling at the time of presentation.

Majority of the patients had lymph nodes enlarged which were less than 2 cm in size, firm, non-tender, discrete and mobile. The children with tuberculosis had matted lymph nodes in all of them but none of them had sinus discharge.

The etiologies in patients with acute lymphadenopathy were tonsillitis orpharyngitis in 27%, Ear infection in 1.96 %, skin infection in 13.7% . In 31 patients, the duration of lymph node swelling was >1 month. The etiologies in those patients were tuberculosis in 54.8% and non- diagnostic hyperplasia in 29%.

Infections in the area of drainage were the predominant causes of cervical lymphadenopathy. Streptococci and staphylococci were the common organisms producing local infections with enlargement of cervical lymph nodes.

Tuberculosis was the leading cause among specific systemic diseases producing chronic cervical lymphadenopathy. Lymphocytosis was commonly observed in this group and was statistically significant (p 0.0004). Chest X Ray was suggestive in 50% cases of tuberculosis while FNAC was suggestive in 70%. Mantoux test and raised ESR were found in all the cases of tuberculosis (10/10) signifying the importance of both in diagnosing tuberculous lymphadenitis.

Microcytic hypochromic anemia (5/10 p=0.0001) and lymphocytosis (3/10 p=0.0004) were significantly present in tuberculous lymphadenitis group in this study while neutrophilia(8/23 p=0.013) was significantly present in local infections causing lymphadenopathy.

Duration of lymph node enlargement, history of weight loss, site and distribution of lymphadenopathy, character of lymph nodes and presence of anemia were found to be of diagnostic value, while approaching a child with cervical lymphadenopathy.

CONCLUSION

Significant pediatric lymphadenopathy is frequently encountered problem in children which requires detailed history and physical examination in arriving for the etiological diagnosis. Most of them are associated with the infections in the drainingof that particular group of lymph of nodes and treatment by appropriate antibiotics is sufficient.

Cervical lymphadenopathy is the most common and can be associated with serious systemic illnesses including Tuberculosis and neoplasms especially when theyare of chronic duration (> 1 month) and when the obvious source of infection is not evident. Detailed investigation work up including CBP, ESR, Peripheral blood smear, Chest X ray, FNAC, Mantoux test along with various serological tests for infectious etiology.

FNAC being simple with minimum complications with good diagnosticaccuracy can be used as a primary diagnostic test in children with significant lymphadenopathy. It is a reliable test in diagnosis of tubercular lymphadenitis especially when used in combination with other tests with high positive predictive values. Further studies and a longer follow up involving detection of antigen, antibodies against lesser known viruses, parasites and investigations for rarer causes of lymphadenopathy may decrease the fraction of many of these undiagnosed reactive hyperplastic conditions.

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