Original Article

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Correlation of Clinical, Sonographical, Fine Needle Aspiration Cytological and Excisional Biopsy Findings in Lymphadenopathy

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Abstract

Aim: To find out the correlation of Clinical Diagnosis and Investigative Techniques, to determine the diagnostic accuracy of Clinical diagnosis, ultrasonography and fine needle aspiration cytology (FNAC) in lymphadenopathy using histopathologic examination of the excised lymph node as gold standard. *Study:* Cross sectional study. Department of Surgery along with Department of Pathology and Department of Radiodiagnostics at Acharya Vinobha Bhave Rural Hospital (AVBRH) attached to Jawaharlal Nehru Medical College (JNMC) which come under Datta Meghe Institute of Medical Sciences (DMIMS) Deemed University.From October 2013 to October 2015. *Material and Methods:* A total of 102 patients suffering from lymphadenopathy were selected. After taking informed consent,the patients were then subject to Ultrasonography and FNAC. Thereafter the same lymph node was removed under local anesthesia for histopathology. All Specimens were sent separately to Cytology and Histopathology units at. Data was analyzed using SPSS version 10. *Result:* 102 patients with a mean age of 35.87 (±17.33) years was sampled, Commonest age group was 41-50 years. the neck was the most common site of lymphadenopathy. The most common cause found for lymphadenopathy was reactive lymphadenopathy followed by tubercular lymphadenitis. clinically size of the lymph node more than 2 cm, duration of more than 2 weeks, consistency and matting were indicators for a neoplastic aetiology. onsonological examination, Longitudinal to transverse ratio, internal echoes and presence of hilum were important finding on ultrasonography to reach at a specific diagnosis. In our study we found that FNAC had a high Specificity (100%) and positive predictive (100%) value in diagnosing secondary metastatic conditions and lymphomas. However in diagnosis of Tubercular lymphadenitis the specificity of FNAC was 81.82% . *Conclusion:* Clinical evaluation of the patient is imperative. Ultrasonography proves to be an important investigative tool that aids in the diagnostic accuracy. Ultrasonography is also important where extent and severity of the disease needs to be identified. FNAC has a high sensitivity and specificity for diagnosis of malignant condition and is useful in those conditions where tissue diagnosis is not required. Where diagnosis is questionable, early excisional biopsy is recommended.

Keywords: Lymphadenopathy; Tuberculosis; FNAC; Secondary Metastasis; Ultrasonography; Clinical Diagnosis.

Introduction

There are approximately 800 lymph nodes in the body and no fewer than 300 of them lie in the neck [1]. Lymphadenopathy is an abnormal increase in size and/or altered consistency of lymph nodes. It is a clinical manifestation of a regional or systemic disease and serves an excellent clue to the underlying disease [2]. Lymphadenopathy can arise from either benign or malignant causes [2].

In review studies done on patients with lymphadenopathy there was 17.5% malignant aetiology including, 11.4% lymphoproliferative disorders and 6.1% metastasis, 31% had reactive benign aetiologies and 34% had other non malignant diseases [3]. Benignaetiologies of lymphadenopathy can include infections, autoimmune disorders, drug hypersensitivity reactions, sarcoidosis, and amyloidosis. A metastatic solid tumour is always in

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the differential diagnosis of localised lymphadenopathy, particularly in older individuals [4, 5].

Nodes are generally considered to be normal if they are up to 1 cm in diameter [6,7]. Nodes need to have a diameter of 22.3 mm or greater to be palpated in 50% of cases [8]. The anatomic location of localised lymphadenopathy will sometimes be helpful in narrowing the differential diagnosis FNA cytology remains the first line of investigations used in cases of lymphadenopathy [9]. Limitations of FNAC include high rate of non diagnostic sampling, high rate of false-negative diagnosis in Hodgkin's disease and incomplete classification of Non-Hodgkin's Lymphoma [10-12]. FNAC is an accurate method in assessing lymphadenopathy [13].

In malignant conditions of lymph nodes, FNAC enjoys a high sensitivity and specificity, the average being 95% [14-17]. FNAC showed a sensitivity of 76.9% in the detection of TB lymphadenopathy [18-22].

High-resolution ultrasonography has been used extensively in the assessment of lymphadenopathy. Ultrasonography (97%) has higher sensitivity than palpation (73%) in the assessment of lymph nodes, and has a high specificity (93%) when combined with ultrasound-guided fine-needle aspiration cytology (FNAC) [23].

Grey scale sonographic features that help to identify metastatic and lymphomatous lymph nodes include size, shape and internal architecture (loss of hilar architecture, presence of intranodal necrosis and calcification). Soft tissue oedema and nodal matting are additional grey scale features seen in tuberculous nodes or in nodes that have been previously irradiated. Power Doppler sonography evaluates the vascular pattern of nodes and helps to identify the malignant nodes. In addition, serial monitoring of nodal size and vascularity are useful features in the assessment of treatment response [24].

When FNAC for Lymphadenopathy results in a non-diagnostic or unequivocal report, open biopsy is frequently performed as the second step in reaching the diagnosis. The advantage of open biopsy is that it nearly always provides a tissue sample sufficient for the diagnosis. However there are many disadvantages like being highly invasive, increased risk of infection, damage to nervous and vascular structures and unfavourable scarring. Open Biopsy also adds cost (because procedure requires the use of an operation theatre), delays diagnosis (because the operation theatre must be scheduled in advance), and carries the risk inherent in sedation or general anaesthesia. Moreover open biopsy carries a known risk of seeding tumour and can violate a future surgical field, making definitive surgical treatment more difficult [25,26].

Our hospital caters to the low socio-economic group and labour class where cost required to reach the diagnosis and time required matters a lot. Clinical evaluation is a must before any investigative modality is used. Yet clinical signs alone may be insufficient in reaching a diagnosis or commencing therapy. Thus selection of an appropriate investigative modality as per the clinical diagnosis will help to achieve this and to reduce the cost burden and loss of valuable time borne by the patient as well as loss of resources by the institution.It is equally necessary to evaluate what additional information these investigations will provide if the clinical diagnosis is pretty sure. It will also help to find out how many Patients have possible dual diseases.

Aims & Objectives

Aim

To find out the correlation of Clinical Diagnosis and Investigative Techniques.

Objectives

To find out clinical and aetiological pattern of lymphadenopathy.

To find out the sensitivity and specificity of Sonography, FNAC and Excisional Biopsy.

To determine a specific investigative technique depending on clinical diagnosis.

Material & Methods

Study Setting

The study will be conducted in Department of Surgery along with Department of Pathology and Department of Radiodiagnostics in a tertiary health care centre Acharya Vinobha Bhave Rural Hospital (AVBRH) attached to Jawaharlal Nehru Medical College (JNMC) which come under Datta Meghe Institute of Medical Sciences (DMIMS) Deemed University.

Duration of Study

From October 2013 to October 2015

Sample size - 100

Study Population

Patients admitted in Surgical, Medical & allied wards or visiting their OPD of AVBRH SAWANGI WARDHA, having Lymphadenopathy are included in our study by applying the following inclusion & exclusion criteria. The study will be conducted during the period from August 2013 to July 2015.

Inclusion Criteria for the Study

Patients with Lymphadenopathyof size more than 1cm6 of any age group with or without symptoms.

Exclusion Criteria

Patient with prior tissue diagnosis available Where Diagnosis has already been reached by other investigative methods.

Ex: A case of leukemia diagnosed on Haematological Evaluation with Lymphadenopathy.

Method

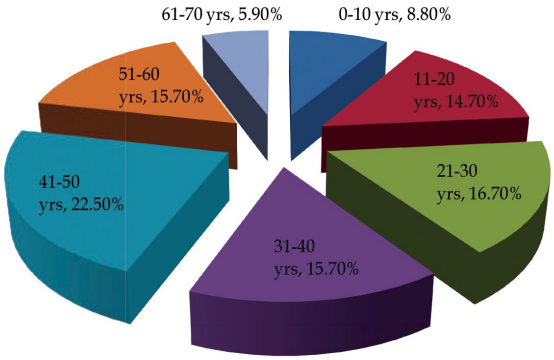
After taking informed consent patients with enlarged lymph nodes are to be included in the study. All patients are to be evaluated Clinically and by Sonographical study. Fine Needle Aspiration Cytology and Excisional Biopsy will be done later. All Specimens are to be sent separately to Cytology and Histopathology units. Each Reporting to be done by separate individuals neither of whom will be informed about the reports of the other investigations.

Observation and Results

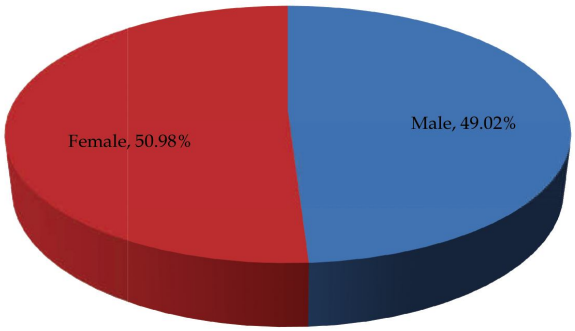
Our study was based at Jawaharlal Nehru Medical College, Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), a rural teaching hospital in Wardha district of Maharashtra state. Between October 2013 and October 2015, we screened a total of 102 patients of all age groups presenting with Lymphadenopathy and they were subject to clinical evaluation, ultrasonography, fine needle aspiration cytology and excision biopsy followed by histopathological examination.

The Dataset comprised of 102 patients with a mean age of 35.87 (±17.33) years, with a range of 0 to 70 years of age. Commonest age group was 41-50 years (22.5%).A total of 102 patients were included in this study. Of the 102 patients 10 (9.8%) of patients were found to have lymphoma, 30 (29.41%), were found to be tuberculous, 21(20.59%) were found to have secondary metastasis and 40 (39.22 %) patients were detected with reactive lymphadenitis. In our study we found that 82.92% of patients of ages upto 30 years, 40% of patients of ages 31 to 60 years and only 16.67% of patients beyond 60 years of age had a benign cause for their lymphadenopathy.

In our study we found that 50 (49.02%) patients were males and 52 (50.98%) were females. The study found no significant gender bias for lymphoma.



Graph 1: Age wise distribution of patients



Graph 2: Sex wise distribution of patients

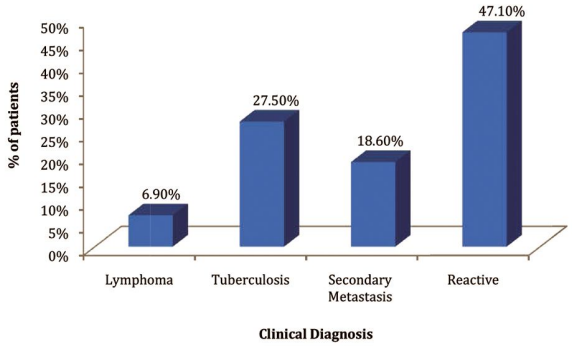
Table 1 shows that the neck was the most common site of lymphadenopathy, 58 (56.86%) of patients presented with cervical lymphadenopathy. Majority of the cases presented with localised (81.37%) lymphadenopathy and a relatively small number presented as generalised (18.62%) lymphadenopathy. 31(30.39%) patients had neoplastic pathology whereas 71 (69.61%) had a non neoplastic aetiology of the localised lymphadenopathy 64 (77.10%) were found to be non-neoplastic and 19(22.89%) were found to be neoplastic. of the 19(18.62%) generalised lymmphadenopathies 12 (63.15%) were found to be neoplastic and 7(36.84%) were non neoplastic. Tuberculosis (4.90%) presented with multiple lymph node enlargement as well and should be kept in mind when making a clinical diagnosis. Lymph node group involved showed statistical significance in distinguishing between neoplastic and non neoplastic groups.

Table 1: Correlation of lymph node involved with Histopathological diagnosis

Diagnosis	Lymphoma	Tuberculosis	Secondary Metastasis	Reactive	Rosai - Dorfman	Total
Submental	0(0%)	2(1.96%)	1(0.98%)	0(0%)	0(0%)	3
Submandibular	1(0.98%)	4(3.92%)	2(1.96%)	11(10.78%)	0(0%)	18
Jugular	3(2.94%)	7(6.86%)	1(0.98%)	14(13.73%)	0(0%)	25
Posterior Triangle	0(0%)	5(4.90%)	1(0.98%)	0(0%)	0(0%)	6
Supraclavicular	0(0%)	3(2.94%)	1(0.98%)	2(1.96%)	0(0%)	6
Axillary	0(0%)	2(1.96%)	3(2.94%)	7(6.86%)	0(0%)	12
Inguinal	0(0%)	2(1.96%)	6(5.88%)	5(4.90%)	0(0%)	13
More than one group involved	6(5.88%)	5(4.90%)	6(5.88%)	1(0.98%)	1(0.98%)	19
Total	10(9.80%)	30(29.41%)	21(20.59%)	40(39.22%)	1(0.98%)	102

2-value

chi=52.16,p-value=0.004,S,p<0.05



Graph 3: Distribution of patients according to clinical diagnosis

Table 2: Distribution of patients according to clinical signs and symptoms

Signs and symtoms	Clinical Signs and symptoms	No of patients	Percentage(%)
Number	Single	58	56.9
	Multiple	44	43.10
Duration	<2 wks	46	45.1
	>2 wks	56	54.9
Size	1-2 cm	68	66.7
	>2 cm	34	33.3
Shape	Round	79	77.5
	Irregular	23	22.5
Matting	Absent	79	77.5
	Present	23	22.5
Surface	Smooth	84	82.4
	Irregular	18	17.6
Consistency	Firm	85	83.3
	Hard	17	16.7
Fixity to surrounding structure	Present	17	16.7
	Absent	85	83.3
Fixity to skin	Present	6	5.9
	Absent	96	94.1
Fever	Absent	83	81.4
	Low Grade	16	15.7
	High Grade	3	2.9
Pain/Tenderness	Present	25	24.5
	Absent	77	75.5
Weight Loss	Present	17	16.7
	Absent	85	83.3

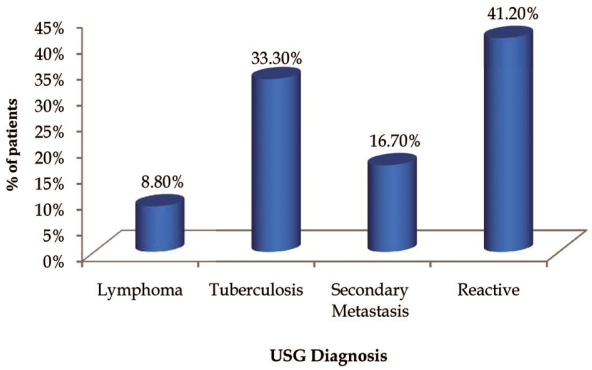
Rashes	Present	12	11.8
	Absent	90	88.2
Cough	Present	15	14.7
	Absent	87	85.3
Dyspnoea	Present	6	5.9
	Absent	96	94.1

In our study we found thatthat on Clinical Examination most of the patients were diagnosed with having reactive lymphadenitis (47.1%) followed by Tuberculosis (27.5%) and Secondary Metastasis (18.6%) with lymphoma (6.9%) as the rarest clinical diagnosis.

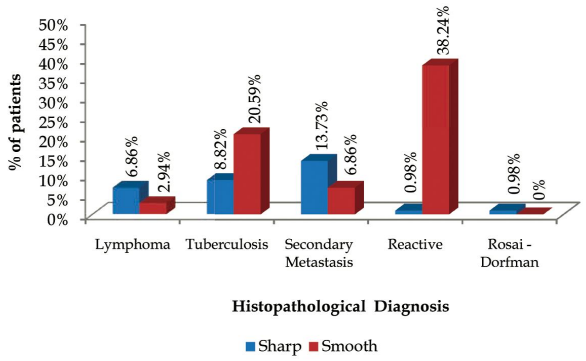
Table 2 shows that 68(66.7%) of patients with lymphadenopathy had lymph node sizes between 1 - 2 cm (66.67%), 51.96% were non-neoplastic and 14.70% were neoplastic. 34(33.33%) of patients had a lymph node size of >2 cm, 15.68% were neoplastic and 26.47% were non-neoplastic. Of the patients with reactive hyperplasia, 87.5% of the cases had a lymph node size of between 1 to 2 cm, while 12.5% of the cases had a lymph node size of more than 2 cm. A consistency of soft to firm was seen in 85(83.3%) of patients and hard consistency was found in 17(16.7%). On comparing the consistency of the lymph nodes all the non neoplastic nodes were soft to firm in consistency where as 51.61% of the neoplastic lymph nodes were hard in consistency. Hard consistency correlated with lymphomas and secondary metastasis. Matting was noted in 23 (22.5%) of nodes and it correlated with tuberculosis, lymphomas and secondary metastasis. In 66.67% of secondary metastasis, 66.67% of tuberculosis and 50% of lumphomas, no matting was found on palpation. In 85 (83.33%) patients the clinically palpable nodes were mobile. Durations of less than 2 weeks was seen in 46 (45.09%) of patients and was associated with a benign aetiology.

In our study we found thaton Ultrasonological Examination Reactive lymphadenitis was seen in 42 (41.2%) and Tuberculosis was found in 34 (23.3%)of cases. Secondary Metastasis was seen in 17 (16.7%) and Lymphoma was seen in 9 (8.8%) of patients.

Distribution of patients according to USG characteristics



Graph 4: Distribution of patients according to USG diagnosis



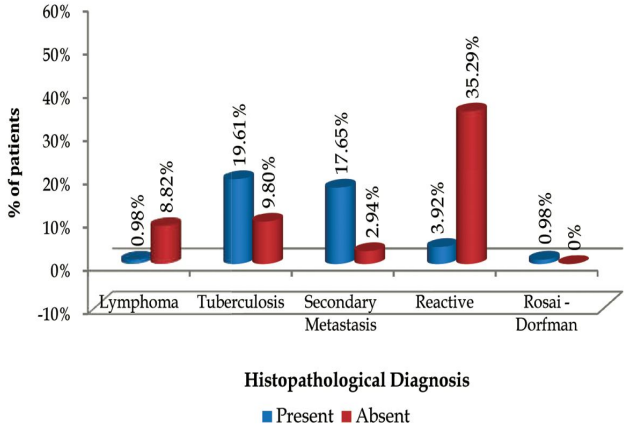
Graph 5: Distribution of patients according to internal echoes

Graph 6 shows that 39(38.24%) with reactive lymphadenitis had smooth borders and 21(20.59%) of patient with tubercular lymphadenitis had smooth borders. 7 (6.86%) of patients with lymphoma and 14 (13.73%) of patients with metastasis had sharp borders. Sharp borders were noted in 14.28% of non-neoplastic and 67.74% of neoplastic cases. Smooth borders were noted in 85.71% of non-neoplastic and 32.25% of neoplastic cases.

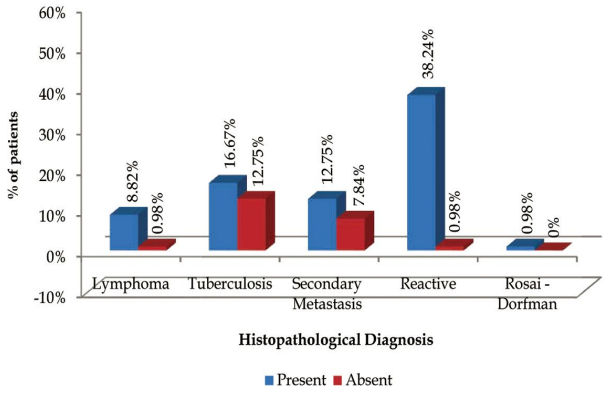
Internal echoes was seen in 20(66.67%) of Tuberculous lymphadenitis and 18(85.71%) of secondary metastasis. absence of internal echoes was seen in 36 (90%) of reactive lymphadenitis and 9 (90%) of lymphomas. The Presence of internal echoes was suggestive of a diagnosis of tuberculosis (45.45%) followed by secondary metastasis (40.90%).

Graph 7 shows that internal echoes were noted in 1 (10%) of lymphoma patients and 8 (39.10%) of secondary metastasis cases. 17(56.67%) of tuberculous lymph nodes and 39(97.5%) of reactive lymph nodes showed presence of echogenic hilum. There was considerable overlap noted between the different groups.

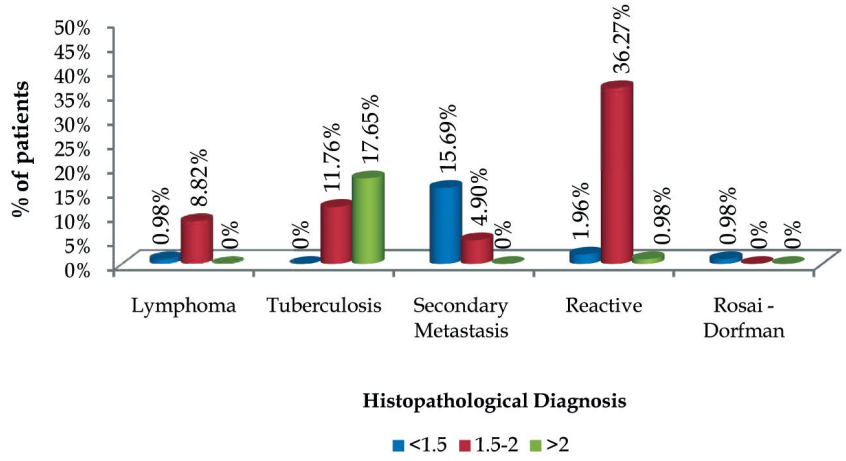
Calcification was seen in 5(4.90%) of lymphomas and 5 (4.90%) of Secondary metastasis. Absent calcification on ultrasound examination was found in 35 (34.31%) of reactive lymphadenitis and 26 (25.49%) of tubercular lymphadenitis. There was no statistical significance between the different groups based on calcification on ultrasonographical examination.



Graph 6: Distribution of patients according to internal echoes



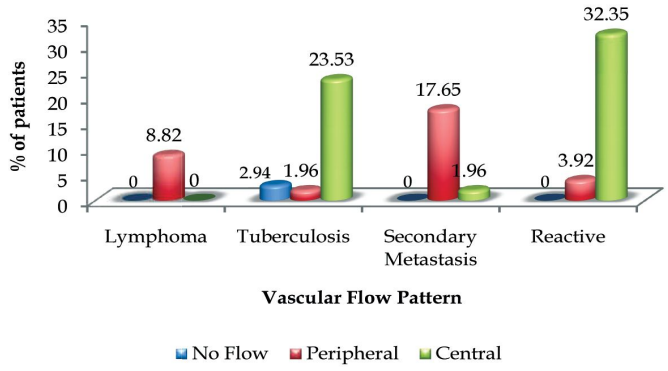
Graph 7: Distribution of patients according to hilum



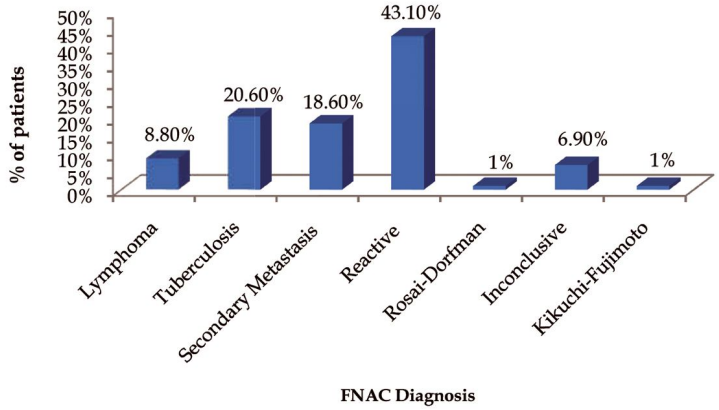
Graph 8: Distribution of patients according to L/T Ratio

A longitudinal to transverse ratio of more than 2 was seen in 18 (60%) of tuberculous lymphadenitis. Secondary metastasis showed a longitudinal to transverse ratio of less than 1.5 in 16(76.19%) of patients and 9 (90%) of patients with lymphoma and 37(92.5%) of patients with reactive lymphadenitis showed a longitudinal to transverse ratio of between 1.5 to 2. There was considerable overlap among different diagnostic groups.

Peripheral Vascular flow was observed in 9(90%) of lymphoma and 18 (85.71%) of patients in secondary metastasis. Central vascular flow was found in 24 (80%) of tuberculous lymphadenitis and 33(82.5%) of reactive lymphadenitis. Thus peripheral vascular flow was seen more commonly in neoplastic (79.41%) cases and central vascular flow was found more commonly in non-neoplastic (96.61%) cases.



Graph 9: Distribution of patients according to vascular flow pattern

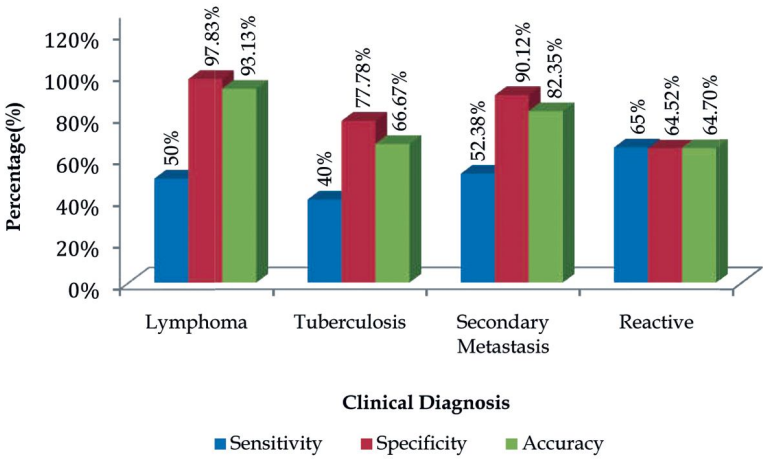


Graph 10: Distribution of patients according to FNAC diagnosis

Fine needle aspiration cytology diagnosed 9 (8.8%) of patients with lymphoma 21(20.6%) of patients with tuberculous lymphadenitis, 19(18.6%) of patients with secondary metastasis and 44 (43.1%) patients with reactive lymphadenitis. 7(6.9%) of the FNACs proved to be inconclusive and 1(0.98%) patient was diagnosed as Kikuchi Fujimoto disease which on histopathology was found to have lymphoma.

Binary Classification of Clinical Diagnosis Versus Histopathological Diagnosis

Binary classification for Clinical diagnosis in Lymphoma revealed a Sensitivity of 50% and specificity of 97.83% with a positive predictive value of 71.43% and an accuracy of 93.13%. Binary classification for Clinical diagnosis in Tuberculosis revealed a Sensitivity of 40% and specificity of 77.78% with a positive predictive value of 42.86% and an accuracy of 66.67%.Binary classification for Clinical diagnosis in secondary metastasis revealed a Sensitivity of 52.38% and specificity of 90.12% with a positive predictive value of 57.89% and an accuracy of 82.35%.Binary classification for Clinical diagnosis in Reactive Lymphadentits revealed a Sensitivity of 65% and specificity of 64.52% with a positive predictive value of 54.17% and an accuracy of 64.70%.



Graph 11: Binary Classification

Binary Classification of USG Diagnosis Versus Histopathological Diagnosis

Binary classification for Ultrasonography in lymphoma revealed a Sensitivity of 60% and specificity of 98.91% with a positive predictive value of 85.71% and an accuracy of 95.09%.Binary classification for Ultrasonography in tuberculous lymphadenitis revealed a Sensitivity of 86.67% and specificity of 88.89% with a positive predictive value of 76.47% and an accuracy of 88.23%.There is an increase in sensitivity (86.67%), specificity (88.89%) and accuracy (88.23%%) over sensitivity (40%),

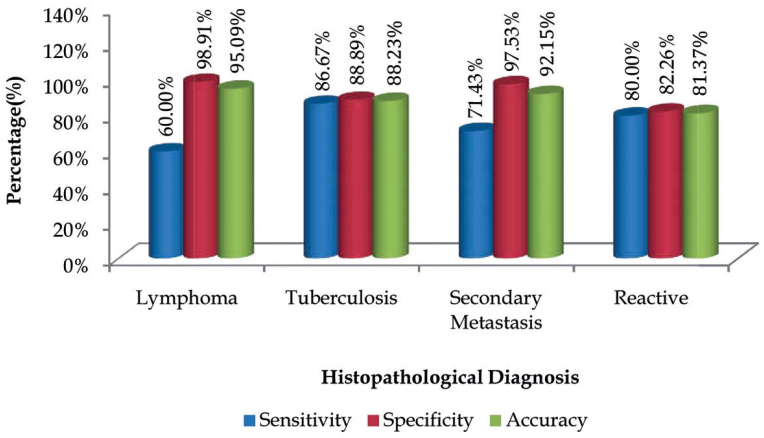
specificity (77.78%) and accuracy (66.67%) of a clinical diagnosis in tuberculous lymphadenitis.Binary classification for Ultrasonography in Secondary metastasis revealed a Sensitivity of 71.43% and specificity of 97.53% with a positive predictive value of 88.24% and an accuracy of 92.15%.Binary classification for Ultrasonography in Reactive lymphadenitis revealed a Sensitivity of 80% and specificity of 82.26% with a positive predictive value of 74.42% and an accuracy of 81.37%.There is an increase in sensitivity (80%), specificity (82.26%) and accuracy (81.37%) over sensitivity (65%), specificity (64.52%) and accuracy (64.70%) of a clinical diagnosis in tuberculous lymphadenitis.

Ultrasonography had a specificity of 80% and accuracy of 81.31% with a specificity of 97.53% in diagnosis of secondary metastasis. there is an increase in the diagnostic accuracy, specificity and sensitivity of ultrasonography over clinical evaluation for identification of tuberculous lymphadenitis and reactive lymphadenitis.

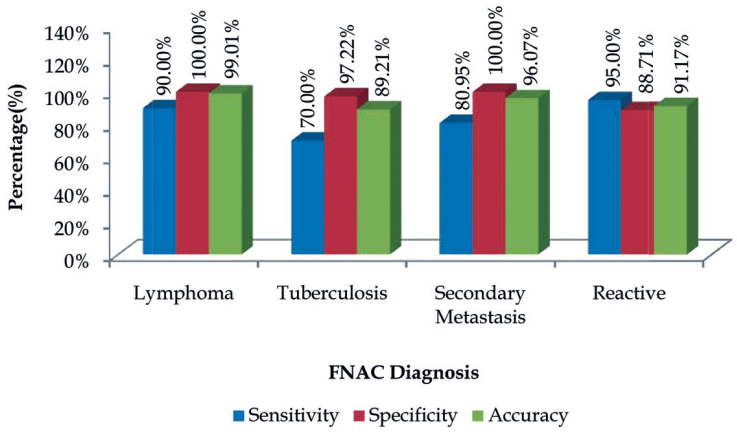
Binary classification for fine needle aspiration cytology in lymphoma revealed a Sensitivity of 90% and specificity of 100% with a positive predictive value of 100% and an accuracy of 99.01%.Binary classification for fine needle aspiration cytology in tuberculous lymphadenitis revealed a Sensitivity of 70% and specificity of 97.22% with a positive predictive value of 91.30% and an accuracy of 89.21%. Binary classification for fine needle aspiration cytology in secondary metastasis revealed a Sensitivity of 80.95% and specificity of 100% with a positive predictive value of 100% and an accuracy of 96.07%.

Binary classification for fine needle aspiration cytology in reactive lymphadenitis revealed a Sensitivity of 95% and specificity of 88.71% with a positive predictive value of 84.44% and an accuracy of 91.17%.

Thus due to its high sensitivity FNAC is a reliable tool for screening of reactive lymphadenopathy. However a negative FNAC report does not rule out other pathologies. FNAC had a high Specificity (100%) and positive predictive (100%) value in diagnosing secondary metastatic conditions and lymphomas. However in diagnosis of Tubercular lymphadenitis the specificity of FNAC was 81.82%.



Graph 12: Binary Classification



Graph 13: Binary classification for FNAC diagnosis

Table 3: Correlation of sensitivity and specificity of clinical, USG and FNAC with histopathological diagnosis

	Clinical Diagnosis		USG Diagnosis		FNAC Diagnosis	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Lymphoma	50%	97.83%	60%	98.91%	90%	100%
Tuberculosis	40%	77.78%	86.67%	88.89%	70%	97.22%
Secondary Metastasis	52.38%	90.12%	71.43%	97.53%	80.95%	100%
Reactive	65%	64.52%	80%	82.26%	95%	88.71%

Discussion

We studied the diagnostic accuracy of clinical signs and symptoms along with clinical judgement and compared it with the accuracy, sensitivity and specificity of investigative modalities of ultrasonography and fine needle aspiration cytology to delineate the pathology of lymphadenopathy and to identify an investigation of choice based on clinical presentation and suspected aetiology.

Age Wise Distribution of Patients

A total of 102 patients were included in this study. Most of study population was in age group between 41 to 50 years of age. Most of study population was middle aged, about 87.5% of patients below 50 years of age. Commonest age group was 41-50 years (22.5%). Least affected age group was above 60 years (5.9%). These finding are comparable to studies by Jha B C et al, Bedi R S et al. and Kim LH et al. However proportion of age group up to 20 year was lesser 23.5% as compared to about 30% as in study by Bedi R S et al [27-29]. In our study we found that 33.26% of patients had a benign cause of lymphadenopathy for ages upto 30 years, 34.3% of patients aged 31 to 60 years and only 9.8% of patients beyond 60 years of age had a benign cause for their lymphadenopathy.

Lee et al [30] analyzed 925 pathology reports from lymph node biopsies done at the Los Angeles County Hospital from 1973-1977 and found that the cause of lymphadenopathy was benign in 79% of the patients under 30, in 59% of the patients aged 31-50 and only 40% of the patients aged 51-80 had a benign cause for their lymphadenopathy.

Gender Wise Distribution of Patients

49.02% patients were males and 50.98% were females. There was no gender bias found in our study in relation to pathology. Most of the studies show female preponderance. About 50.98% of population in this study comprised of females. studies done by Purohit S.D. et al. And Tripathy S et al found results similar to this study [31].

Lymph Node Involvement

In our study we found that the neck was the most common site of lymphadenopathy, 58 (56.86%) of patients presented with cervical lymphadenopathy. Majority of the cases presented with localised (81.37%) lymphadenopathy and a relatively small number presented as generalised (18.63%) lymphadenopathy. 31 (30.39%) patients had neoplastic pathology whereas 71 (69.61%) had a non neoplastic aetiology. Of the localised lymphadenopathy 64 (77.10%) were found to be non-neoplastic and 19 (22.89%) were found to be neoplastic. Of the 19 (18.62%) generalised lymphadenopathies 12 (63.15%) were found to be neoplastic and 7 (36.84%) were non neoplastic. Tuberculosis (4.90%) presented with multiple lymph node enlargement as well and should be kept in mind when making a clinical diagnosis. Lymph node group involved showed statistical significance in distinguishing between neoplastic and non neoplastic groups. Although localised lymph node enlargement does not rule out malignancy. Generalised and progressive lymphadenopathy often indicates a significant disease.

Karadeniz and colleagues reported that pyogenic infections more frequently manifested with localised lymphadenopathy, while non infectious causes like Hodgkin's and non-Hodgkin's lymphoma (NHL) and Secondaries frequently manifested with generalised lymphadenopathy. Nohaet al noted that all cases presenting as isolated axillary, inguinal, and mediastinal lymphadenopathy had a non-neoplastic aetiology. Among the 30 cases presenting with generalised lymphadenopathy involving the peripheral lymph node groups, 21 cases were non-neoplastic (70%), and among the 27 cases presenting with generalised lymphadenopathy involving both peripheral and central lymph node groups, 17 cases were neoplastic (63%). Chhabra and colleagues16 found in their study that most common site of lymph node involvement was neck. Shaik and colleagues10 described that posterior group of lymph node was most commonly affected in Tubercular lymphadenitis (49.5%).

Clinical Diagnosis

In the Present Study we noted that on Clinical Examination most of the patients were diagnosed

with having reactive lymphadenitis (47.1%) followed by Tuberculosis (27.5%) and Secondary Metastasis (18.6%).

Mohan et al [32] in their study found that the majority (35.6%) of these patients had non-specific lymphadenitis. Tuberculous lymphadenitis (31.3%) was the second most common cause followed by Secondary Metastasis (25.9%).

Clinical Signs and Symptoms

In our study we found that of the patients with lymph node size between 1 - 2 cm (66.67%), 51.96% were non-neoplastic and 14.70% were neoplastic. Of the patients with a lymph node size of >2 cm (33.33%), 15.68% were neoplastic and 26.47% were non-neoplastic. Of the patients with reactive hyperplasia, 87.5% of the cases had a lymph node size of between 1 to 2 cm, while 12.5% of the cases had a lymph node size of >2 cm. Most of the palpable lymph nodes (83.3%) were soft to firm in consistency as compared to proportion of hard lymph nodes (16.7%). On comparing the consistency of the lymph nodes all the non neoplastic nodes were soft to firm in consistency where as 51.61% of the neoplastic lymph nodes were hard in consistency. Hard consistency correlated with lymphomas and secondary metastasis. Matting was noted in 77.5% of nodes and it correlated with tuberculosis, lymphomas and secondary metastasis as final diagnosis. 83.33 % of clinically palpable nodes were mobile and fixity was associated with malignancy. Durations of less than 2 weeks was seen in 45.09% of patients and was associated with a benign aetiology. that These findings are comparable to classical finding described in literature.

Noha et al noted that out of the 48 cases with a lymph node size of between 1 to 2 cm, 79.2% were non-neoplastic and 20.8% were neoplastic. Out of the 51 cases with a lymph node size of >2 cm, 52.9% were neoplastic and 47.1% were non-neoplastic. In the group of reactive hyperplasia, 60% of the cases had a lymph node size of between 1 to 2 cm, while none of the cases had a lymph node size of >2 cm. By comparing the consistency of the lymph nodes all the non-neoplastic nodes were soft to firm in consistency where as 8.3% of the neoplastic lymph nodes were hard in consistency. Hard consistency correlated with lymphomas and secondary metastasis. Matting was noted in 15.83% of lymph nodes. Fixedlymph nodes were found only in the neoplastic category. A significant difference was found related to the duration of symptoms where a duration of less than 2 weeks suggested a non-neoplastic course.

UItrasonographic Characteristics

Lymph Node Borders

Smooth borders on ultrasonographical examination correlated with a non-neoplastic (85.71%) aetiology whereas sharp borders correlated with a neoplastic (67.74%) aetiology. Reactive (38.24%) and tuberculosis (20.59%) cases had predominantly smooth borders whereas lymphoma (6.86%) and secondary metastasis (13.73%) had predominantly sharp borders. This was comparable with the literature given below.

In tuberculosis, node borders are not sharp probably due to active inflammation of the surrounding soft tissues. Malignant nodes (including metastases and lymphoma) tend to have sharp borders, whereas benign nodes usually do not have such sharp borders. Similar results were reported by Ahuja and Ying where 94% of metastatic cervical lymph nodes had sharp nodal borders and 100% of reactive cervical lymph nodes had smooth nodal borders Esenet al also found similar results in their studies.

Internalechoes

The Presence of internal echoes was suggestive of a diagnosis of tuberculosis (19.61%) followed by secondary metastasis (17.65%). However the absence of Internal echoes does not rule out an underlying pathology. This when compared with literature showed similar results.

Asai et al reported that strong internal echoes and echogenic thin layer were characteristic of tubercular cervical lymphadenopathy. The echogenic thin layer histopathologically corresponded to a specific granuloma tissue layer surrounding a caseous necrosis. It is to be noticed that hypoechoic mass is the common finding described in the literature as characteristic of tubercular lymphadenopathy [25]. Tuberculous nodes are predominantly hypoechoic, which is probably related to the high incidence of intranodal cystic necrosis. The metastatic nodes are usually hypoechoic as reported by Lindeboom et al when compared with the adjacent muscles. However, metastatic nodes from papillary carcinoma of the thyroid tended to be hyperechoic. Lymphomatous nodes were reported to have a 'pseudocystic appearance' and hypoechoic with posterior enhancement.

Intranodal Hilum

In our study we found that the presence of intranodal echogenic hillus was observed in

predominantly reactive lymphadenopathy (38.24%) followed by tubercular lymphadenopathy (16.67%). However an echogenic hills was found in lymphoma (8.82%) and Secondary metastasis (12.75%) as well. Presence of echogenic hilum did not rule out malignancy however absence of echogenic hilum must cause a suspicion of malignancy.Therefore, the presence / absence of an echogenic hilus within lymph nodes should not be the sole criterion in the evaluation of cervical nodes.

The presence of an intranodal echogenic hilus was considered a sign of benignity. Previous studies have reported that 84–92% of benign nodes demonstrate an echogenic hilus. However, 4–51.5% of metastatic nodes may also have an echogenic hilus. Therefore, the presence / absence of an echogenic hilus within lymph nodes should not be the sole criterion in the evaluation of cervical nodes. In an Indian study for paediatric age group, hilum was present in 73.53% tubercular lymphadenitis 40% lymphoma and 62.5% cases with metastatic lymph nodes. Hypo-echoic centre was present in 88.24% tubercular lymphadenitis cases followed by 62.5% metastatic and 60% malignant lymphoma cases.

Longitudinal to Transverse Ratio

An L/T ratio more than 2 was indicative of tuberculosis and a smaller L / T ratio correlated with malignancy however there was considerable overlap among different diagnostic groups.

Steinkamp HJ et al report that 95% of metastatic nodes had L/T ratio of less than 2.116 Similar findings were recorded in an Indian study for paediatric age group echogenic thin layer and strong internal echoes were identified as specific for tuberculosis. Long axis to transverse axis ratio was more than 2 in most of the tubercular nodes (85.71%). Hilum was present in 73.53% tubercular lymphadenitis 40% lymphoma and 62.5% cases with metastatic lymph nodes. Hypoechoiccentre was present in 88.24% tubercular lymphadenitis cases followed by 62.5% metastatic and 60% malignant lymphoma cases. *Chang et al.* noticed that benign lymph nodes had a significantly larger Longitudinal to Transverse ratio than did malignant nodes Na D G et al noticed that Longitudinal to Transverse ratio <2 had a sensitivity of 85% and a specificity of 61% for malignancy, which has not been supported by *Moritz et al* .

Vascular Flow Pattern

In our study we found that there Peripheral Vascular flow was observed more commonly in lymphoma(90%) and secondary metastasis (85.71%) cases. Central vascular flow was found more commonly in tuberculous (80%) lymphadenitisand reactive (82.5%) lymphadenitis. Thus peripheral vascular flow was seen more commonly in neoplastic (79.41%) cases and central vascular flow was found more commonly in non-neoplastic (96.61%) cases.

Gupta and Colleagues has reported that power Doppler ultrasonographic evaluation of the vascular pattern of cervical nodes is highly reliable with a repeatability of 85%. In the normal neck, about 90% go lymph nodes show hilar vascularity. Normal and reactive lymph nodes tend to demonstrate hilar vascularity or appear apparently avascular. However, metastatic lymph nodes usually have a peripheral or mixed vascularity. The presence of peripheral vascularity in malignant nodes is thought to be related to tumour angiogenesis and the associated recruitment of capsular vessels. Because peripheral vascularity is common in malignant nodes, its presence, regardless of the presence or absence of hilar vascularity, is highly suggestive of malignancy. On ultrasound, tuberculous nodes have varied vascular pattern, which simulates both benign and malignant conditions. In spite of the varied vascular pattern, displaced vascularity and apparent avascularity are common in tuberculous nodes, which are related to the high incidence of cystic necrosis in tuberculous lymph nodes as was reported by Ahuja and colleagues.

The ultrasonographical characteristics showed considerable overlap in the various pathologies. Vascular pattern and Longitudinal to transverse ratio were important finding on ultrasonography to reach at a specific diagnosis. However since there was considerable overlap between the various finding, no significant association emerged regarding which of these factors or combinations of these factors were important in diagnosing an underlying disease. The association of USG characteristics and specific diagnosis is comparable to studies by Chang et.al and Asai et.al.

Binary Classification of Clinical Diagnosis Versus Histopathological Diagnosis

In our study we noted that clinical diagnosis had an accuracy of 93.13 for lymphoma and 82.35 for Secondary metastasis however the diagnostic accuracy for tuberculosis was 66.67 and reactive lymphadenitis was 64.70.

An increase in the specificity and accuracy was seen in the clinical diagnosis of lymphoma as most patients present late when the disease has advanced

usually aiding clinical diagnosis however the low diagnostic accuracy seen in tuberculous and reactive lymphadenitis is due to the paucity of clinical sings and symptoms associated with the disease making clinical judgement inadequate.

Binary Classification of Ultrasonography Diagnosis Versus Histopathological Diagnosis

In our study we found that Ultrasonography had a specificity of 80% and accuracy of 81.31% with a specificity of 97.53% in diagnosis of secondary metastasis.There is an increase in sensitivity (86.67%), specificity (88.89%) and accuracy (88.23%%) over sensitivity (40%), specificity (77.78%) and accuracy (66.67%) of a clinical diagnosis in tuberculous lymphadenitis. and sensitivity (65%), specificity (64.52%) and accuracy (64.70%) of a clinical diagnosis in reactive lymphadenitis. Ultrasonography did aid in diagnostic accuracy however in many instances it provided diagnostic clues that were inconclusive.

Andrea Frasoldati et al [34] reported the presence of metastatic lesions was confirmed in 46 of 95 patients with suspicious neck nodes. Ultrasonography sensitivity and specificity were 82.1% and 91.2%, respectively. D B Chang and colleagues [35] found 16 benign lymph nodes (four were tuberculous lymphadenitis, four were reactive hyperplasia, and eight were unspecified) and 32 malignant lymph nodes (13 were squamous cell carcinomas, nine were adenocarcinomas, four were small-cell carcinomas, three were lymphomas, and three were miscellaneous. Colour Doppler flow patterns were seen in six (38%) of the 16 benign lymph nodes and in 29 (91%) of the 32 malignant lymph nodes.

Ultrasonography as a diagnostic modality in lymphadenopathy does confer an added benefit in improving the overall accuracy of diagnosis due to its increased sensitivity and specificity over clinical judgement, however ultrasonography alone may not be sufficient as the diagnostic investigation of lymphadenopathy as a tissue diagnosis would still be mandatory before initiation of therapy. Where clinical diagnosis is certain ultrasonography confers little advantage to the diagnosis and where the clinical diagnosis is questionable ultrasonography may prove useful in improving diagnostic accuracy yet it will require a tissue diagnosis for confirmation. Even so the utility of sonography will always be preserved in identifying the extent of the disease.

Binary Classification of FNAC Diagnosis Versus Histopathological Diagnosis

In our study we found that FNAC had a high Specificity (100%) and positive predictive (100%) value in diagnosing secondary metastatic conditions and lymphomas. However in diagnosis of Tubercular lymphadenitis the specificity of FNAC was 81.82% which is comparable with the literature. Due to its high sensitivity FNAC is a reliable tool for screening of reactive lymphadenopathy. however a negative FNAC report does not rule out other pathologies.

In a study by Dong Hoon and Colleagues, the sensitivity, specificity, positive-predictive value, negative-predictive value, and accuracy for diagnosing pediatric lymphadenopathy was 100, 75, 93.3, 100, and 94.4%, respectively. These values suggest that FNAC is an accurate method in assessing lymphadenopathy [15]. Fine needle aspiration cytology (FNAC) has been used extensively for the diagnosis of primary and secondary malignant disorders involving lymphnodes, though the same does not hold true for non-neoplastic disorders. Engzell and colleagues 17 reported that Sensitivity and specificity of cytology approaches 95% and 96.5% respectively specially in diagnosis malignant conditions. However in a study by S. K. Lauaet al [24] FNAC showed a sensitivity of 76.9% in the detection of TB lymphadenopathy.

Fine Needle Aspiration Cytology is a minimally invasive, simple economical and quick procedure that is easily carried out in the out patient department or at the bed side. it is useful in the preliminary evaluation of superficial lymphadenopathy. As a result of its high sensitivity and specificity and due to its high diagnostic accuracy FNAC is useful in those conditions where tissue is not required for further evaluation. Though FNAC has a relatively high sensitivity and specificity in diagnosis of lymphoma, tissue will be required for further evaluation in the form of immunohistochemistry and thus FNAC falls short of an excisional biopsy followed by histopathological evaluation. However it should be made clear that a negative FNAC does not rule out the pathology. The accuracy of FNAC in reactive lymphadenitis is comparatively low.

It is always very difficult to make an accurate diagnosis in the early stages of the disease. As the disease advances the clinical features get more pronounced and thus aids in accuracy of clinical diagnosis. As our patients are rural based and come late due to referrals from primary health centers or due to socio economic reasons, the clinical accuracy is more. In such a situation one can always select an investigation according to the clinical diagnosis. Thus

reducing unnecessary investigations, its cost burden and time spent before definitive therapy can be commenced.

The real problem remains when reactive lymph nodes are encountered. Clinical examination and investigations such as ultrasonography and FNAC may not contribute much to the diagnostic accuracy. Empirical lymph node biopsy may be warranted in such situations, failing which there is a chance that an underlying pathology may be missed as patients seldom turn up for regular follow up. Most of these patients have been provided primary care with antibiotic regimens before they seek care at a tertiary care center. Considering these factors it is justified in doing a lymph node biopsy before an antibiotic trial at a tertiary institute if lymphadenopathy is significant at the time of presentation. In our study we have found that 45.83% patients diagnosed clinically as reactive to have false positive values. Biopsy is thus the best modality to reach to a diagnosis in clinically reactive lymph nodes.

Summary and Conclusion

This prospective study of 102 patients on correlation of clinical, sonographical, fine needle aspirationcytological and excisional biopsy findings in Lymphadenopathy is based in a tertiary health care centre rural teaching hospital.

Clinical evaluation of the patient is imperative. Most patients withlymphadenopathyare in the age groups between 41 to 50 years with no male or female preponderance. Cervical group of lymph nodes are the most commonly involved group. Among all clinical features, consistency, group of lymph nodes involved, duration and presence of matting correlates strongly with the final diagnosis.

Standard clinical examination has high diagnostic accuracy. It also provides diagnostic clues for further evaluation. However in manycases a diagnosismay not be established on clinical judgement alone.

In cases where the clinical judgement is suspect ultrasonography proves and important investigative tool that aids in the diagnostic accuracy, however ultrasonography alone may not be sufficient to make a diagnosis and will require tissue diagnosis for confirmation. Ultrasonography is also important where extent and severity of the disease needs to be identified.

The ultrasonographical characteristics showed considerable overlap in the various pathologies. Vascular pattern and Longitudinal to transverse ratio were important finding on ultrasonography to reach at a specific diagnosis. However since there was considerable overlap between the various finding, no significant association emerged regarding which of these factors or combinations of these factors were important in diagnosing an underlying disease. Ultrasonography improved diagnostic accuracy in non neoplastic conditions like tuberculosis and reactive lymphadenitis.

Fine needle aspiration cytology is simple, economical and minimally invasive procedure that can easily be carried out in the out patient setting or at the patients bed side. FNAC is useful in the preliminary evaluation of superficial lymph node enlargements. FNAC has a high sensitivity and specificity for diagnosis of malignant condition and is useful in those conditions where tissue diagnosis is not required.

The most common cause found for lymphadenopathy was reactivelymphadenopathy followed by tubercularlymphadenitis.

To conclude, for most patients presenting with lymphadenopathy clinical evaluation must precede any and all investigations. If however a suspicion of lymphoma is made clinically the patient must be subject to excision biopsy and histopathology as despite high specificity of other modalities immunohistochemistry will be required.

If malignancy is suspected clinically FNAC can be preferred over biopsy.

Ultrasonography is an important tool in identifying extent of disease but offers little to establish a diagnosis. Tubercular and reactive lymphadenitis requires multiple modalities of investigative techniques bearing in mind that a negative report does not rule out a pathology.

Limitations

Clinical diagnosis alone is suspect in cases that tend to present early with low symptomology. Subjectivity of the clinician is also an important factor in varying diagnostic accuracy of a clinical diagnosis.

Ultrasonography is a subjective investigation and user dependant. Thus the findings may vary resulting in a varied diagnostic accuracy. Ultrasonography alone may not be sufficient as the diagnostic investigation of choice for lymphadenopathy as a tissue diagnosis would still be mandatory before initiation of therapy. Where clinical diagnosis is certain ultrasonography confers little advantage to the diagnosis and where the clinical diagnosis is questionable ultrasonography may prove useful in

improving diagnostic accuracy yet it will require a tissue diagnosis for confirmation.

Microscopic evaluation of the FNAC slides depends on many factors like the experience of the reporting cytopathologist, the clinical information, good technique of aspiration, adequacy of material, well made and well stained smears, and gross observations made at the time of aspiration.

Though FNAC has a relatively high sensitivity and specificity in diagnosis of lymphoma, tissue will be required for further evaluation in the form of immunohistochemistry and thus FNAC falls short of an excisional biopsy followed by histopathological evaluation. However it should be made clear that a negative FNAC does not rule out the pathology. The accuracy of FNAC in reactive and tubercular lymphadenitis is comparatively lower.

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