Evaluation of Lymph Node Biopsy: A Five-YearReview of the Value of Lymph Node Biopsies in a Tertiary Health Facility in North Eastern Nigeria

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ABSTRACT

Background: *Several diseases are associated with lymph node enlargement either as primary lesion or secondary to other disease conditions. It is essential to define the pattern of disorders presenting as lymph node enlargement in an environment.*

Methods: *We reviewed the histopathological diagnosis of biopsied lymph nodes from patients who presented to University of Maiduguri Teaching Hospital between 2010-2015. The demographic variables were sex, age in years and defined age group. The research variables were site and cause of lymphadenopathy. Retrieved histopathological results considered were those in which tissues were processed, stained with haematoxylin and eosin (H&E), and examined by a specialist.*

Results: *Of the available records of 145 patients retrieved and considered, cervical lymph nodes were the most biopsied region. Tuberculous (TB) adenitis lesions, 43 (29.7%) constituted the commonestcases, it was followed by secondary metastasis, 39 (26.9%) and 36 (24.8%) cases of reactive hyperplasia. The proportion of Hodgkin's and non-Hodgkin's lymphoma was 16 (11.0%) and 11 (7.6%) respectively. There was progressive increase in mean ages ± SD, from reactive hyperplasia (22.4±18.2) to TB adenitis (27.1±14.2) to non –Hodgkin's (29.5±21.3) to Hodgkin's (36.8±20.4)to secondary metastatic lesion (43.0±18.6), p = 0.001.*

Conclusion: *This study indicate that tuberculosis is the most common cause of lymph node enlargement; followed by secondary metastatic lesions especially among adults and the elderly. Cervical lymph nodes are the most frequently enlarged region irrespective of the underlying cause of the enlargement.*

Keywords: *Lymphadenopathy, TB adenitis, Histopathology, Northeastern Nigeria.*

INTRODUCTION

Lymph node enlargement remains a common feature of several diseases seen in clinical practice. The causes range from inflammatory conditions to malignancy. Superficial lymphadenopathy due to tuberculosis and other infectious agents is common in tropical and sub-tropical regions[1].This is in sharp contrast to developed regions where lymphadenopathy is often due to malignant conditions and other non-infectious diseases[1]. Due to wide

range of diseases that may cause lymphadenopathy, it is essential to document causes of lymph node enlargement in a particular environment[2].Unfortunately, determination of the cause of lymph node enlargement on clinical grounds is often difficult due to overlapping nature, pattern and trend among its differential diagnosis.

Evaluation of lymph node enlargement remains a herculean task in several heath facilities in developing countries due to dearth of facility and expertise for histopathological diagnosis. Over-lap of nonneoplastic and neoplastic lesions that may require information from studies other than H&E light microscopy. Lack of sophisticated and newer tests, especially immune and genetic markers poses diagnostic challenge in evaluating lymph node pathologies[3]. Morphologic examination of paraffin sections of lymph node tissue biopsy, however still remains the standard method of establishing lymph node diagnosis in developing countries[4,5].

Several reports indicate tuberculosis and other infectious etiology as a major causes of lymph node enlargement in developing countries[6,7].Increase in incidence of tuberculosis is attributed to the lingering preponderance of HIV infection, low socioeconomic status and substandard health infrastructure[8,9]. Considering the plethora of diseases that may cause lymphadenopathy, determination of its causes, including documentation of the contribution of tuberculosis, a fairly common disease in developing countries and pattern of lymph node enlargement is necessary.

Against this background, we reviewed the records of histopathological diagnosis of biopsied lymph nodes from 2010 -2015 as seen in a tertiary health facility in northeastern Nigeria.

MATERIALS AND METHODS

This study is a retrospective study of lymph node biopsies conducted in the department of Histopathology, University of Maiduguri Teaching Hospital. Archived lymph node biopsy report of cases over a period of 5 years, from January 2010 to December 2015 were retrieved and reviewed.

Lymph node biopsy records of 145 patients that had complete information were considered for evaluation. Histology slides of all cases were reviewed and clinico-demographic data regarding age, sex, anatomical site of nodal biopsy and clinical information were obtained from histology request forms and register. All biopsies were fixed in 10% formalin and routine hematoxylene-eosin stained sections were examined. Special stains like Ziehl-Neelsen and Periodic Acid-Schiff stains were employed where necessary. Only one biopsy per patient was included. Results were interpreted in respect of age, sex, site of lymphadenopathy and histopathological diagnosis. Diagnosis of tuberculosis was confirmed by demonstration of epithelioid granuloma with caseation necrosis on histopathological examination. Non-Hodgkin lymphomas (NHLs) were classified based on working formulation.

The results were tabulated and presented as percentages and frequencies. Means and standard deviations (SD) were used to summarize continuous variables, while percentages were used for categorical

variables. Biopsy results with incomplete records such as biodata and clinical information were excluded from this study.

RESULTS

Records of 145 patients that had diagnostic excisional biopsy of enlarged lymph node between 2010 -2015, were considered in this study. The mean age ± standard deviation, (min -max) of the studied patients was 31.35 ±19.24, (1 – 100) years. A total of 79 (54.5%) cases were non-neoplastic, while 56 (45.5%) were neoplastic lesions. Of the non-neoplastic cases consisting of reactive hyperplasia and Tuberculous (TB) adenitis, most cases 80.6% and 81.4% respectively were seen among those aged < 40 years. Conversely 26 (66.7%) of those that had secondary metastatic lesion were aged ≥ 40 years as presented in Table 1.

Table 1: Age distribution of histological types of lymphadenitis

Age range (years)	*Reactive hyperplasia*	*Tuberculous adenitis*	*Non Hodgkins Lymphoma*	*Hodgkins Lymphoma*	*Secondary Metastasis*
0 - 9	10 (27.8%)	03 (07.0%)	03 (27.3%)	02 (12.5%)	01 (02.6%)
10 - 19	09 (25.0%)	11 (25.6%)	02 (18.2%)	03 (18.8%)	03 (07.7%)
20 - 29	08 (22.2%)	10 (23.3%)	01 (09.1%)	02 (12.5%)	04 (10.3%)
30 - 39	02 (05.6%)	11 (25.6%)	00 (00.0%)	02 (12.5%)	06 (15.4%)
40 - 49	02 (05.6%)	03 (07.0%)	02 (18.2%)	03 (18.8%)	11 (28.2%)
50 - 50	03 (08.3%)	04 (09.3%)	02 (18.2%)	00 (00.0%)	07 (18.0%)
-	02 (05.6%)	01 (02.3%)	01 (09.1%)	04 (25.0%)	07 (18.0%)
Total	36 (100%)	43 (100%)	11 (100%)	16 (100%)	39 (100%)

Stratification of cases based on gender indicates that the proportion of males, 88 (60.7%) was higher than females, 57 (39.3%), with male: female ratio of 1.5:1. TB adenitis lesions, 43 (29.7%) constituted the highest cases, this was followed by secondary metastasis, 39 (26.9%) and 36 (24.8%) cases of reactive hyperplasia. The proportion of Hodgkins and non-Hodgkins lymphoma was 16 (11.0%) and 11 (7.6%) respectively. There is no difference in mean ages and proportion based on gender among different disease entities as depicted in Table 2.

Table 2: Mean ages and proportion of cases stratified by sex

	Reactive hyperplasia	*Tuberculous adenitis*	*Non hodgkins Lymphoma*	*Hodgkins Lymphoma*	*Secondary Metastasis*
Mean ages ± SD	22.44±18.21	27.07±14.18	29.46±21.34	36.81±20.41	42.97±18.61
Females	27.00±20.90	26.74±14.18	32.00±25.87	29.25±15.63	40.63±12.37
Males	19.19±15.72	27.33±14.49	28.50±21.34	38.00±21.93	44.61±22.07
Proportion (%)	36 (24.8%)	43 (29.7%)	11 (07.6%)	16 (11.0%)	39 (26.9%)
Females, no (%)	15(41.7%)	19 (44.2%)	03 (27.3%)	04 (25%)	16 (41%)
Female :Male	1:1.4	1:1.3	1:2.7	1:2	1:1.4
p-value[1]	0.209	0.893	0.823	0.450	0.515
p-value[2]	0.519	0.654	0.497	0.233	0.436

Legend: p[1] Mean statistical significant between Males and Females within a group p[2] Statistical significance in proportion between Males and Females within a group. Figure 1 Shows the mean ages of the cases based on histological diagnosis. There was an observed progressive increase in mean ages ± standard deviation, from reactive hyperplasia (22.4±18.2) to TB adenitis (27.1±14.2) to non –Hodgkin's (29.5±21.3) to Hodgkin's (36.8±20.4) to secondary metastatic lesion (43.0±18.6), p = 0.001.

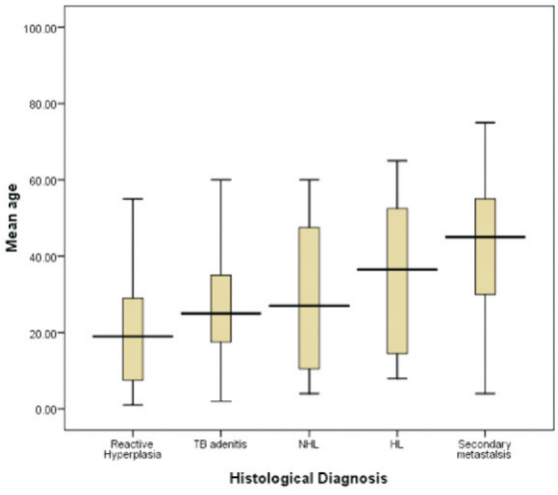

Figure 1:Mean ages of cases based on histological diagnosis

Lymph nodes group in the cervical region was the commonest site of involvement of all

the lesions seen among cases with the exception of reactive hyperplasia that showed a higher predilection for mesenteric lymph nodes. TB adenitis involving the cervical group of lymph node was the commonly involved region in this study. The distribution of the histopathologic lesions based on sites of involvement is as presented in Figure 2.

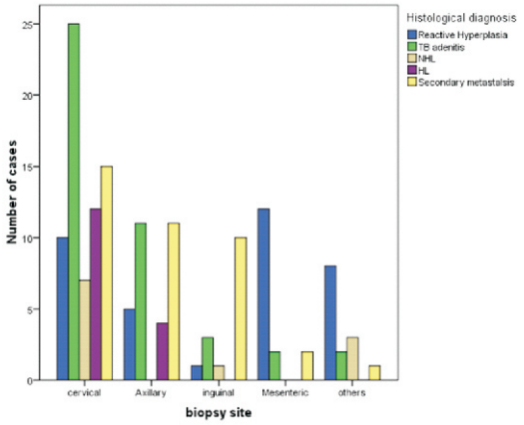

Figure 2 Distribution of cases based on biopsy site.

As shown in Figure 3, the distribution of cases within a defined age group stratified by gender indicates that TB adenitis was commoner among cases aged ≥ 10 years and < 40 years irrespective of gender. Reactive hyperplasia was commoner among cases aged <20 years in both males and females. Secondary metastasis was rare among females aged < 20 years but peaked from 4th decade in both sexes. Hodgkins lymphoma was commoner among those aged 10 -19 years and ≥60 years among males.

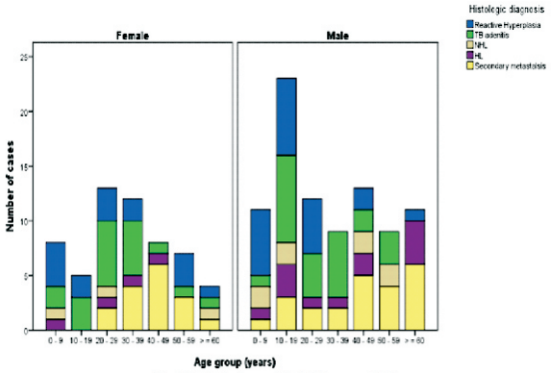

Figure 3: Distribution of cases within defined age group stratified by sex

DISCUSSION

Lymph node enlargement is a common presentation in clinical practice. It is caused by several conditions ranging from infectious and inflammatory conditions to malignant conditions. It is desirable to promptly ascertain its etiology to avoid morbidity and mortality associated with delayed management of infectious agents such as tuberculosis and malignant conditions. Although Fine needle aspiration cytology (FNAC) is a valuable test used in evaluating lymph adenopathy[10], excisional biopsy is the gold standard due to sub optimal sensitivity and specificity of FNAC[11]. In this study, tuberculosis was the most common cause of lymph node enlargement constituting 29.7% of cases. This finding agrees with several previous studies that indicated infectious agents especially tuberculosis as the common cause of lymphadenopathy in developing countries[5,12,13] and malignancy in developed countries[14,15]. Several factors such as low socioeconomic status, inefficient health care to detect and treat tuberculosis, scourge of HIV infection is responsible for the burden of tuberculosis in developing countries[9,16,17.] Conversely, malignancy has been documented as the major cause of lymph node enlargement in the developed

countries[17]. Low incidence of tuberculosis and earlier detection of malignancies before the onset of nodal metastasis may be the explanation for the prominence of reactive hyperplasia as a more common cause in the western world[17].

A study conducted in the South eastern Asia[18], Middle East[19] and eastern Africa[20]also indicates tuberculosis as the commonest cause of lymphadenopathy. Several previous National studies conducted in North Eastern[21], Central[6], Western[22]and South Western[23], Eastern[5] and South Southern Nigeria[12] corroborated our finding. The proportion of TB was similar between females and males in this report. This is in contrast to previous studies conducted in Nigeria[29] and other developing countries[19]. The mean ages of participants diagnosed with TB adenitis in this study was 27.1years, it was higher than with mean age of 24.2yearsobtained from similar report from southeastern Nigeria [29]. Most similar studies from developing nations reported high incidence of TB within the reproductive age group[19-23].

Enlarged lymph nodes in the cervical region was the most frequently biopsied in this study, this is in tandem with most other studies done both within[5,6,12, 21-23] and outside Nigeria[19,20]. The finding of TB as most common cause of adenopathy, often with predilection for the cervical region in our study and most studies in developing region reflect high TB burden. Several studies have also reported TB adenitis involving the cervical region as a common form of extrapulmonary TB in endemic nations[24-34]. This is however, in contrast with studies from Turkey [35] and Parkistan[36] that reported intrathoracic and supraclavicular region as a common cause of TB adenitis. Furthermore, in patients with generalized or regional adenopathy, cervical region is early accessible for excisional biopsy. This may explain why it was the most biopsied region in this study. Generally, peripheral nodes in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than lower limb nodes (popliteal, inguinal or femoral) as the former are more likely to yield definitive diagnosis whereas the latter are often characterized by non-specific reactive or chronic inflammatory and fibrotic changes[1,30,37].

Lymphadenopathy in children and young adults are usually due to benign and reactive etiologies; in contrast, in people older than 50, prevalence of malignant etiologies increases[1]. Of the non-neoplastic cases constituting of reactive hyperplasia and TB adenitis, most cases 80.6% and 81.4% respectively were seen among those aged < 40 years in this report. Our finding is similar to previous studies [19-24] that reported lymphadenopathy to be common in the first three decades of life; with preponderance of reactive lymphadenopathy in early years of life, TB within reproductive age group and malignancy among adult and the elderly[1,14, 20-24]. The reason for more common reactive lymphadenopathy in children has been adduced to a reaction to minor stimuli because of the yet developing immune system [24,25]. In the United States of America, reactive hyperplasia is most common cause of lymphadenopathy [1,14]. The lower prevalence of tuberculosis and earlier detection of malignancies before the onset of nodal metastasis may be the explanation for the prominence of reactive hyperplasia as a

more common cause in the western world [14]. Lymph node hyperplasia was reported to be common in earlier study by Anunobi*et al* in Lagos, south west Nigeria[26] and similar studies conducted in regions with high incidence of HIV infection[4,7,9]. Lymph node hyperplasia occur due to several pathological processes including HIV infection[1]. The trend of changes in primary HIV lymphadenopathy ranges from mild follicular hyperplasia through diffuse follicular hyperplasia to "burnt out lymph node"[1,8].

In our study, metastasis accounted for 39(26.9%) of the cause of lymphadenopathy. This is similar to the finding from southeastern Nigeria[5], but lower than reports from South Western Nigeria [12,23,27], yet significantly higher than 2.6% reported from South Africa[4] and 12.4% by Sibanda *et al* from Zimbabwe[31]. In western countries such as United States, the incidence of infections including TB is rare, however, high incidence of malignant conditions such as metastasis has been reported to be high[28]. Previous studies have reported metastatic lesion to account for as high as 29% of lymph node enlargement[26,27].

Lymphomas constituted 27(18.6%) of lymphadenopathy in this study. It is similar to a previous study conducted in Nigeria by Oluwale *et al*[23] but lower than 63.3% by Sincliar *et al*[33] from United States and 35% by Amir from Saudi Arabia [34]. In our study, the prevalence of Hodgkin's 16(11%) was higher than non Hodgkin's 11 (7.6%). It was in contrast to a Nigerian study by Olu-Eddo *et al*[30] and a study reported from India by Mohan *et al*[31] that reported a higher preponderance of non-Hodgkin's lymphoma. In western world, non-Hodgkin's lymphoma is reported to be three to four times more common than Hodgkin's Lymphoma[28]. The high preponderance of NHL in literatures emanating from the western world could be partially explained by racial and genetic factors[28].

Determination of the spectrum of clinical conditions associated with lymph node enlargement in a particular environment is necessary. Knowledge of differential diagnosis can assist to guide clinicians on the possible etiology of lymph node pathologies. Lymph node biopsy remains an important and valuable diagnostic tool in evaluation of lymph node enlargement as it allows for the architecture of the gland to be viewed thereby giving an accurate and concise diagnosis with minimal risk to the patient. Prompt diagnosis is valuable to avert morbidity and mortality associated with managing advanced malignancies and disseminated infectious agents.

Limitations

The study is a retrospective one with its attendant limitation in that microbiological aspect of the study was not done. Data was retrieved from the database of patients. Evaluation of biopsied specimen to establish diagnosis was achieved through morphologic examination of paraffin sections.

CONCLUSION

This study indicate that tuberculosis is the most common cause of lymph node enlargement in our setting; followed by secondary metastatic lesions especially among adults and the elderly. Cervical lymph nodes are the most frequently enlarged region irrespective of the underlying cause of the enlargement.

Recommendations

There is need to update pathology laboratories in developing countries with modern diagnostic facilities such as immunohistochemistry, cytogenetics and molecular diagnostic techniques like lymphocyte receptor gene rearrangements to increase their diagnostic efficiency.

REFERENCES

1. Henry P, Longo D. Enlargement of lymph nodes and spleen. In: Kasper D,Braunwald E, Fauci A, Hauser S, Longo D, Jameson L. Harrison's principles of internal medicine. 19th ed. New York: McGraw Hill. 2015; 1102 - 1105.
2. Abba AA, Khalil MZ. Clinical approach to Lymphadenopathy. JK Practitioners. 2011; 16(1-2): 1 – 8.
3. Özkan EA, Göret CC, Özdemir ZT, Yanık S, Göret NE et al. Evaluation of peripheral lymphadenopathy with excisional biopsy: six-year experience. Int J Clin Exp Pathol. 2015;8(11):15234-15239.
4. Moore SW, Schneider JW, Schaaf HS. Diagnostic aspects of cervical lymphadenopathy in children in the developing world: a study of 1,877 surgical specimens. Paediatric Surg Int. 2003; 19: 240-244.
5. Mbata GC, Nweke IG, Egejuru RO, Omejua EG, Nwako OF. South Eastern Histologic Pattern of Lymph Node Biopsies in a Tertiary Hospital in Nigeria. J AIDS Clin Res2015; 6: 475. doi:10.4172/2155-6113.1000475
6. Obafunwa JO, Olomu IN, Onyia NJ. Primary peripheral lymphadenopathy in Jos, Nigeria. West Afr J Med. 1992;11(1): 25-28.
7. Thomas JO, Ladipo JK, Yawe T. Histopathology of lymphadenopathy in a tropical country. East Afr Med J. 1995; 72(11): 703-705.
8. Robbins S, Cotran R. Diseases of the immune system. In: Kumar V, Abbas AK, Sausto N, Aster JC (eds). Robbins and Cotran pathologic basis of disease. 8th edn. Philadelphia: Elsevier Saunders. 2010: 235-249.
9. Bem C, Patil PS, Bharucha H, Namaambo K, Luo N. Importance of human immunodeficiency virus associated lymphadenopathy and tuberculous lymphadenitis in patients undergoing lymph node biopsy in Zambia. Br J Surg. 1996; 83(1): 75-78.
10. Reddy DL, Venter WDF, Pather S. Patterns of Lymph Node Pathology; Fine Needle Aspiration Biopsy as an Evaluation Tool for Lymphadenopathy: A Retrospective Descriptive Study Conducted at the Largest Hospital in Africa. PLoS ONE. 2015; 10(6): e0130148. doi:10.1371/journal.pone.0130148.
11. Moor JW, Murray P, Inwood J, Gouldesbrough D, Bem C. Diagnostic biopsy of lymph nodes of the neck, axilla and groin: rhyme, reason or chance? Ann R Coll Surg Engl. 2008; 90: 221–225.
12. Olu-eddo AN, Omoti CE. Diagnostic evaluation of primary cervical adenopathies in a developing country. Pan Afr Med Jour. 2011; 10:52
13. GC Kamat. A ten-year histopathological study of generalized lymphadenopathy in India, South African Family Practice. 2011; 53:3, 267-270.
14. Freidig EE, McClure SP, Wilson WR, Banks PM, Washington JA. Clinical-histologic-microbiologic analysis of 419 lymph node biopsy specimens. Clin Infect Dis. 1986; 8(3): 322-328.
15. Sriwatanawongsa V, Cardoso R, Chang P.

Incidence of malignancy in peripheral lymph node biopsy. Am Surg 1985. 51(10): 587-590.
16. Narang P, Narang R, Mendiratta DK, Sharma SM, Tyagi NK. Prevalence of tuberculous lymphadenitis in children in Wardha district, Maharashtra State, India. Int J Tuberc Lung Dis. 2005 9(2): 188-194.
17. Chakraborty AK. Epidemiology of tuberculosis: current status in India. Indian J Med Res. 2004; 120: 248-276.
18. Tiwari M, Aryal G, Shrestha R, Rauniyar SK, Shrestha HG. Histopathologic diagnosis of lymph node biopsies. Nepal Med Coll J. 2007; 9:259-61.
19. Abba AA, Bamgboye AE, Afzal M, Rahmatullah RA. Lymphadenopathy in adults. A clinicopathological analysis. Saudi Med J. 2002; 23:282-6.
20. Getachew A, Demissie M, Gemechu T. Pattern of histopathologic diagnosis of lymph node biopsies in a teaching hospital in Addis Ababa, 1981-1990 G.C. Ethiop Med J. 1999;37:121-7.
21. Pindiga UH, Dogo D, Yawe T. Histopathology of primary peripheral lymphadenopathy in North Eastern Nigeria. Niger J Surg Res. 1999; 1:69-70
22. Ochicha O, Edino ST, Mohammed AZ, Umar AB, Atanda AT. Pathology of peripheral lymph node biopsies in Kano, Northern Nigeria. Ann Afr Med. 2007; 6:104-8.
23. Oluwole SF, Odesanmi WO, Kalidasa AM. Peripheral lymphadenopathy in Nigeria. Acta Trop. 1985; 42:87-96.
24. Lake AM, Oski FA. Peripheral lymphadenopathy in childhood- Ten-year experience with excisional biopsy. Am J Dis Child. 1978; 132 (4):357-9.
25. Adelusola KA, Oyelami AO, Odesanmi WO, Adeodu O. Lymphadenopathy in Nigerian children. West Afr J Med. 1996; 15 (2): 97-100.
26. Anunobi CC, Banjo AA, Abdulkareem FB, Daramola AO, Abudu EK. Review of the histopathologic patterns of superficial lymph node diseases, in Lagos (1991-2004) Niger Postgrad Med J. 2008;15:243–6.
27. Akinde OR , Anunobi CC , Abudu EK , Daramola AO , Banjo AA , Abdulkareem FB , Osunkalu VO Pattern of lymph node pathology in Lagos. Nigerian Quarterly Journal of Hospital Medicine. 2011, 21(2):154-158.
28. Hertge P, Devess SS, Fraumeni JF. Hodgkin's and non-Hodgkins lymphoma. Cancer Surv. 1994;19:423-433.
29. Ukekwe FI, Olusina DB, Banjo A, Akinde OR, Nzegwu MA, Okafor OC, et al. Tuberculous lymphadenitis in South-Eastern Nigeria; A 15 years histopathologic review (2000-2014). Ann Med Health Sci Res. 2016;6:44-9.
30. Olu-Eddo AN, Ohanaka CE. Peripheral lymphadenopathyin Nigerian adults. J Pak Med Assoc. 2006; 56(9): 405-408.
31. Mohan A, Reddy MK, Phaneendra BV, Chandra A. Aetiology of peripheral lymphadenopathy in adults: analysis of 1724 cases seen at a tertiary care teachinghospital in Southern India. Natl Med J India. 2007; 20(2): 78-80.
32. Sibanda EN, Stanczuk G. Lymph node pathology in Zimbabwe: a review of 2194 specimen. Q J Med. 1993; 86(12): 811 - 817.
33. Sinclair S, Beckman E, Ellman L. Biopsy of enlarged superficial lymph nodes.JAMA. 1974;228(5):602-604.
34. Amr SS, Kamal MF, Tarawneh MS. Diagnostic value of cervical lymph

nodebiopsy: a pathological study of 596 cases. J Surg Oncol. 2006;42(4):239-243.
35. Ilgazli A, Boyaci H, Basyigit I, Yildiz F. Extrapulmonary tuberculosis: clinical and epidemiological spectrum of 636 cases. Arch Med Res. 2004; 35(5): 435-441.
36. Khan KN,Javed A and Ahmad A. Lymph node diseases: a histopathological analysis of 86 cases at tertiary care teaching hospital in Peshawar.Pak J Chest Med. 2005;11(2):9-12.
37. Rosai J. Lymph nodes. In: Rosai and Ackerman's Surgical Pathology. 9th edn. St. Louis: Elsevier Mosby. 2004: 1878-1888.