

The Profile of Lymphadenopathy in Adults and Children

H K Darnal, M.D, N Karim, K Kamini, FRCPath, MRCPATH, K Angela

Department of Pathology, Royal College of Medicine Perak, No. 3, Jalan Greentown, Ipoh, Perak, Malaysia

Summary

Surgical biopsies of lymphnodes of 315 patients (273 adult and 42 children) were reviewed microscopically and analysed. The sex ratio was similar in adults but in children males were twice than female (2:1). Ethnically Malay patients predominated in both the groups. The commonest cause of biopsied lymphadenopathy in adults were malignancy (47%) followed by chronic nonspecific lymphadenitis (20%) and granulomatous lymphadenitis (9%) while in children chronic nonspecific lymphadenitis was the commonest (46%) followed by granulomatous lymphadenitis (21%) and malignancy (14%). Twenty percent of adults and 4% of children had normal lymphnodes. Secondary deposits in adult males and females were of squamous cell carcinoma and adenocarcinoma type respectively. In our study 100% of children and 96% of adults with granulomatous lymphadenitis had tubercular lesions.

Key Words: Lymphnode, Malignancy, Granulomatous, Adult, Childhood

Introduction

The human body has approximately 600 lymph nodes. The submandibular, axillary or inguinal lymphnodes may normally be palpable in healthy people¹. Nodes are packed with lymphocytes that are organized into cortical nodules and medullary cords by connective tissue, trabecule and lymphatic sinuses². Lymphadenopathy refers to nodes that are abnormal in either size, consistency or number^{3,4}. It is usually caused by multiplication of cells normally residing within the node in response to foreign antigens or by invasion or propagation of either inflammatory or neoplastic cells into the node².

Evaluation of patients with lymphadenopathy requires a thorough history and physical examination. Lymphadenopathy is described as a node larger than 1cm, although this varies according to the specific site. Palpable supraclavicular, iliac or popliteal lymphnodes of any size or epitrochlear larger than 0.5 cm or

inguinal nodes larger than 1.5 cm should be considered as abnormal^{5,6}. Stony hard nodes are typically a sign of cancer usually metastatic. Firm, rubbery nodes suggest lymphoma. Softer nodes are results of infection or inflammation. Nodes that are matted can be either benign (tuberculosis, sarcoidosis) or malignant (metastatic carcinoma, lymphoma)³. Pain is usually the result of an inflammatory process, suppuration or haemorrhage into the necrotic center of a malignant node. Generalised lymphadenopathy is defined as lymphadenopathy found in two or more distinct anatomical region. Antigenic stimulation of the immune responsive cells of lymph nodes increases as age advances. Hence, the incidence of lymphadenopathy in adults is much more than in infants and children. Depending on the antigens, the pattern of lymphadenopathy in children are different than in the adults. However, there are no records of such data in our environment according to our knowledge. We therefore, decided to look into the lymph node pathology from this angle.

This article was accepted: 25 May 2005

Corresponding Author: Darnal Hari Kumar, Department of Pathology, Royal College of Medicine Perak, No. 3, Jalan Greentown, Ipoh, Perak, Malaysia

Aim

The aim of this study was to compare the features of lymphadenopathies in adults and children. The main objectives were to determine the demographic parameters and the clinical presentation of the various causes of lymphadenopathy in adults and children.

Materials and Methods

All patients who had undergone a lymph node biopsy in General Hospital Ipoh between January 2001 to December 2003 were evaluated. Patients aged 18 years and below were categorized as children and those above 18 years as adults. The cases were identified through review of the histopathological report and records from the Pathology Department. The case notes were then retrieved from the Surgical, ENT and Medical Departments for collection of relevant data. Demographic parameters, clinical presentation at diagnosis, size and sites of node swelling were recorded. After review of 315 patient's data, a comparative study was done. The recorded information was then entered in SPSS 12.0 for Windows and the results were evaluated.

The lymphadenopathy were classified into 7 main categories, as follows:

1. Acute Nonspecific Lymphadenitis
2. Chronic Nonspecific Lymphadenitis
3. Granulomatous Lymphadenitis
4. Infective Lymphadenitis
5. Dermatopathic Lymphadenitis
6. Neoplastic - Primary : Non-Hodgkin's lymphoma and Hodgkin's lymphoma
- Secondary
7. Normal

Results

A total of 344 patients were subjected to a lymph node biopsy between 2001 to 2003. Twenty-nine cases were excluded from this study due to faulty biopsies or misdiagnoses such as lipomas and paraganglioma. Therefore, a total of 315 patients were included in this study, 273 adults (87%) and 42 children (13%) with sex ratio of 1:1 among adults and 2:1 among children (Fig 1).

The ethnic distribution among the adults were Malays - 51%, Chinese - 32%, Indians - 16% and Orang Asli - 1%. However, the ethnic distribution among children, were of Malays (62%) followed by Indians (17%), Chinese (14%) and Orang Asli (7%). (Fig 2).

Analysis of the causes of lymphadenopathy between 2001-2003 were obtained from 273 adults and 42 children. The commonest cause among adults was malignancy (47%) followed by Chronic NonSpecific Lymphadenitis (20%) and Granulomatous Lymphadenitis (9%). Out of the total, 20% of the adult patients had normal results. The commonest cause of lymphadenopathy in children was Chronic NonSpecific Lymphadenitis (46%) followed by Granulomatous Lymphadenitis (21%) and Malignancy (14%). Only 4% of the children had normal lymph nodes. Other causes of lymphadenopathy in adults and children are shown in Fig 3.

Malignancy

It was the most common cause of lymphadenopathy in the adults. Primary malignancy constituted 35% whereas secondary malignancy, 65%. Fig. 4

Out of the 45 adult patients with primary malignancy, 34 had Non - Hodgkin's Lymphoma and 11 had Hodgkin's Lymphoma. The majority of adults who had Non-Hodgkin's Lymphoma were males (71%), Malay (65%), with a node size ranging from 2-2.5cm comprising (55%). Majority presented with generalized lymphadenopathy (53%). Five histological types of Non-Hodgkin's lymphoma identified, were Diffuse T-Cell type (44%), Diffuse B-Cell type (38%), Lymphocytic B-Cell type (12%), Anaplastic type and Follicular B-Cell type (3% each).

The clinical presentation of the 34 patients diagnosed with Non-Hodgkin's Lymphoma are listed in Fig. 5.

The adults diagnosed with Hodgkin's Lymphoma were mainly males (73%) and the racial distribution was equal among Malays (37%) and Chinese (36%) and the remaining (27%) were Indians. The size of lymph nodes were mostly in the range of 2 - 2.5cm. Generalized, (46%), cervical (45%) and inguinal, (9%) were the sites of enlarged lymph nodes present in these 11 patient. The Clinical Manifestation and Histological types are shown in Figures 6 and 7.

According to our data, 4 children had Primary Malignancy, 2 were diagnosed with Hodgkin's Lymphoma and the other two, Non-Hodgkin's Lymphoma. A total of 85 adults had secondary malignancies, the majority were Carcinomas followed by Undifferentiated tumours and Sarcoma (Fig 8). Only two children had secondary malignancy, both were undifferentiated tumours.

Two major types of carcinoma found among the adults with secondary malignancies, were adenocarcinoma followed by squamous cell carcinoma (Fig:9).

The majority of adults who had adenocarcinoma were female (81%), Malay (46%), with a size ranging from 2-2.5cm comprising 37%. Majority presented with axillary swelling (66%). The primary sites of adenocarcinoma are mainly from the breast (71%) followed by the gastrointestinal tract (18%), the lung (9%) and kidneys (2%). The most common histological type of adenocarcinoma was infiltrating ductal carcinoma (79%) followed by clear cell type (9%), mucinous type (6%), infiltrating lobular carcinoma (4%) and large cell type (2%).

Adults who were diagnosed with squamous cell carcinoma were mostly male (80%), Chinese predominance (40%), with a size ranging from 2-2.5cm comprising 41%. Majority presented with cervical lymphadenopathy (73%). The primary sites of squamous cell carcinoma are mainly from the lung (46%) followed by the tongue (23%), the penis (15%) and the skin and nasopharynx (2%) respectively.

Granulomatous Lymphadenitis

A total of 25 adults had Granulomatous Lymphadenitis, 96% were tuberculosis and the remaining 4%, stitch granuloma. Out of the 9 children with granulomatous lymphadenitis, all were diagnosed as tubercular lymphadenitis. The majority of patients with tuberculosis were male (71%) in adults and (56%) in children. (Fig 10).

The highest distribution among adults with tuberculosis were Malay (62%) followed by Chinese (21%), Indians (13%) and Orang Asli (4%). However, among the children majority were Malay (45%) followed by Orang Asli (33%) and Chinese (22%) (Fig 11).

The most common size of enlarged lymph node found in 54% of adults and 78% of children were in the range of 1.1-1.5cm. The commonest site of lymph node swelling in adults with tuberculosis was cervical lymphnode (75%) followed by generalized

lymphadenopathy (10%), supraclavicular (10%) and inguinal (5%) whereas in children generalized lymphnode enlargement (60%) supraclavicular (20%) and cervical (20%).

Clinical presentation of adults and children with tuberculosis are shown in Figures 12 and 13.

Acute Non Specific Lymphadenitis

A total of 3 patients were found to be in this category and all of them were children.

Chronic Non Specific Lymphadenitis

A total of 54 adults had Chronic Non Specific Lymphadenitis with a male to female ratio of 1:1. The racial distribution predominated by Malays (52%) followed by Chinese (35%) and Indians (13%). The most common size of enlarged lymph node found in 55% of adults were in the range of 1.1-1.5cm. Cervical lymphadenopathy (54%) was commonly seen among the adults. Other sites of lymphnode swelling were axilla (27%), submandibular (11%), inguinal (5%) and occipital (3%). The various histological types of chronic non specific lymphadenitis were sinus histiocytosis (50%), follicular hyperplasia (48%) and paracortical hyperplasia (2%).

The clinical presentation seen in adults with Chronic Non Specific Lymphadenitis are listed in Fig 14.

According to our data collection, 19 children had Chronic Non Specific Lymphadenitis with an overall male to female ratio of 2:1. The racial distribution predominated by Malays (69%) followed by Indians (21%), Chinese and Orang Asli found to be equal, 5%. The most common size of enlarged lymph node found in 57% were in the range of 1.1-1.5cm. Cervical lymphadenopathy (82%) was the most common site of swelling seen in children followed by inguinal (9%) and generalized lymphnode swelling (9%).

The majority histological type is follicular hyperplasia (74%) and the remaining (26%) were sinus histiocytosis.

The clinical presentation of children with Chronic Non Specific Lymphadenitis are shown in Fig 15.

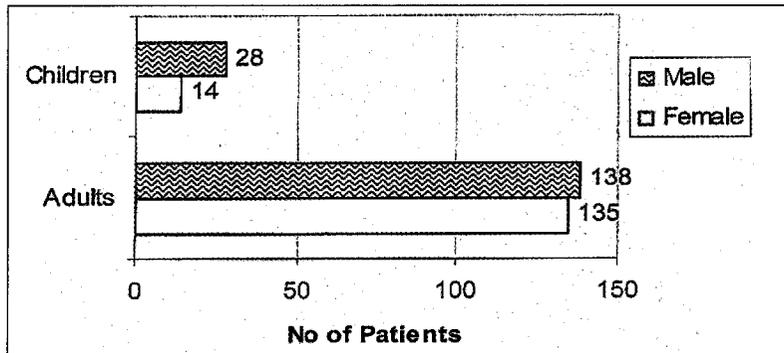


Fig. 1: The gender distribution among patient's who has a lymph node biopsy done between 2001-2003

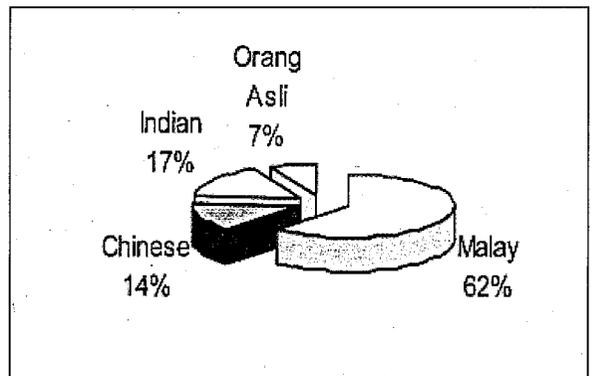
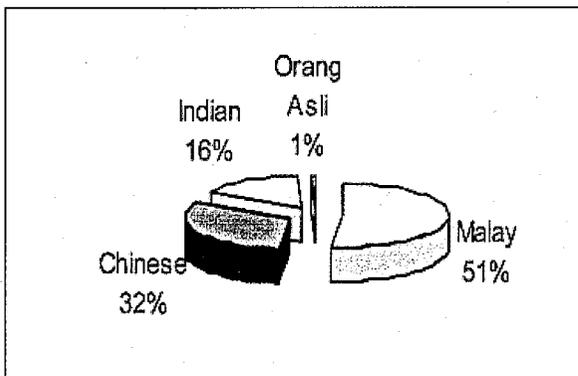


Fig. 2: The ethnic distribution among adults and children who had a lymph node biopsy done between 2001-2003

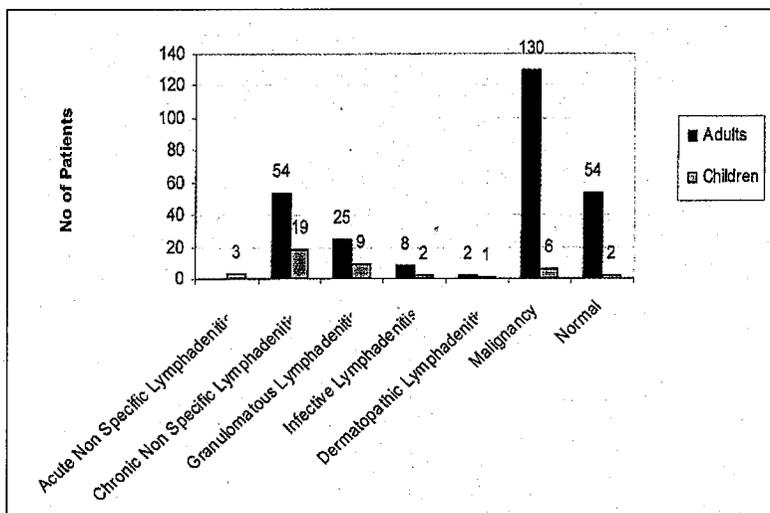


Fig. 3: The causes of lymphadenopathy seen among adults and children between 2001-2003

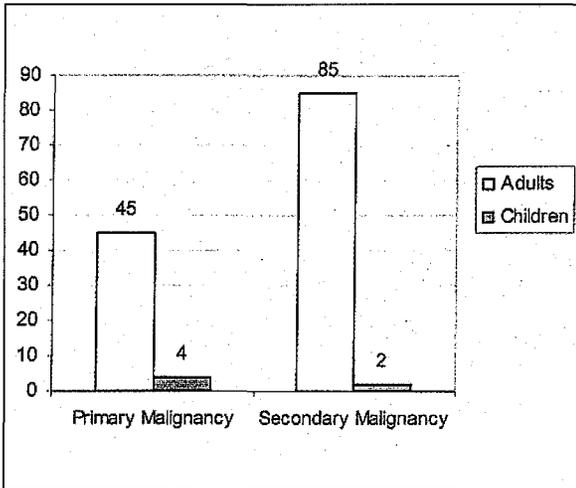


Fig. 4: Breakdown of neoplastic causes of lymphadenopathy in patients between 2001-2003

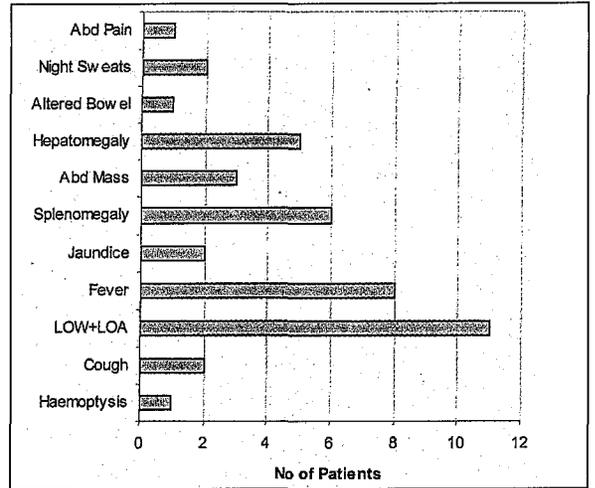


Fig. 4: Clinical presentation of adults with NHL (n=34)

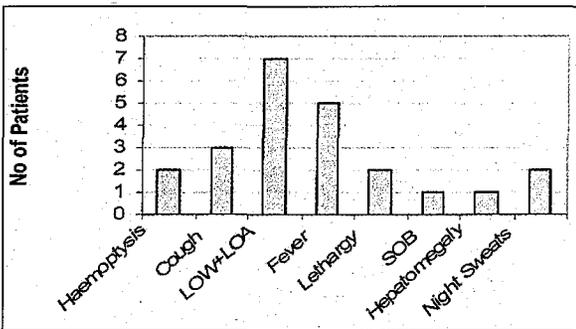


Fig. 6: Clinical presentation of adults with HL (n=11)

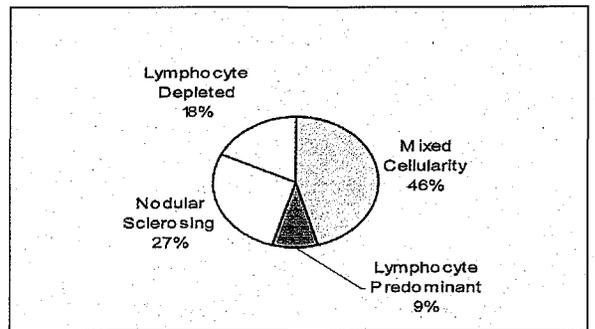


Fig. 7: Histological types of HL in adults (n=11)

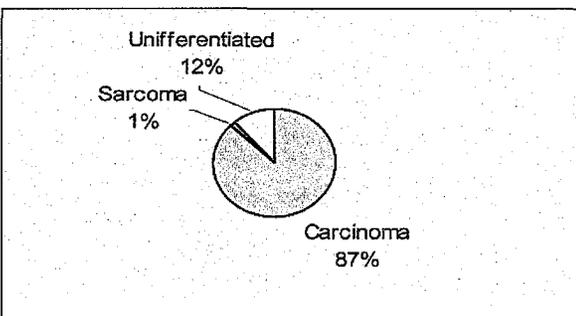


Fig. 8: The major categories of secondary malignancy in adults with lymphadenopathy between 2001-2003 (n=85)

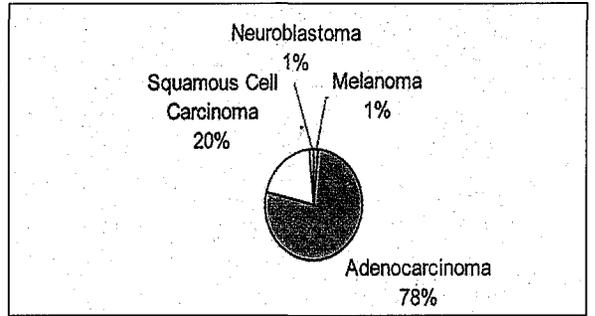


Fig. 9: The types of carcinoma in adults with lymphadenopathy between 2001-2003

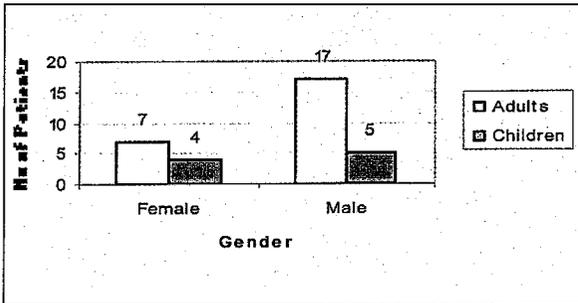


Fig. 10: Gender distribution among adults and children with tuberculosis

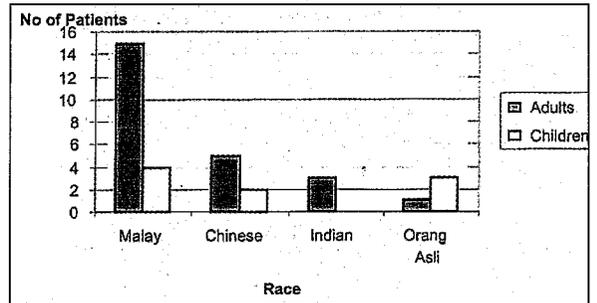


Fig. 11: Ethic distribution among adults and children with tuberculosis

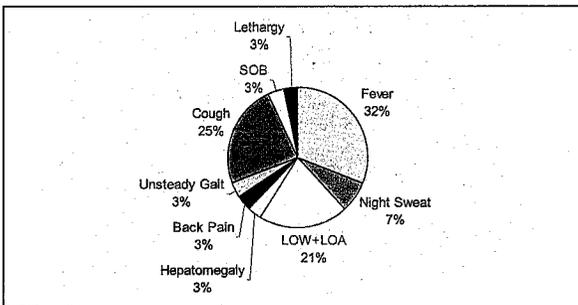


Fig. 12: Clinical presentation of adults with tuberculosis

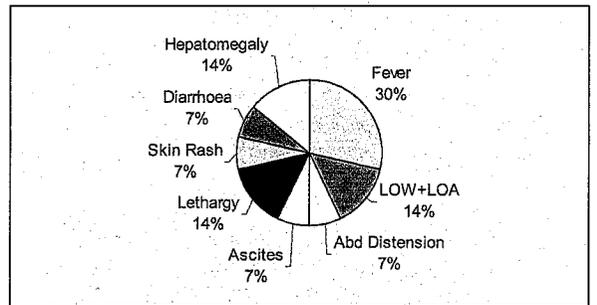


Fig. 13: Clinical presentation of children with tuberculosis

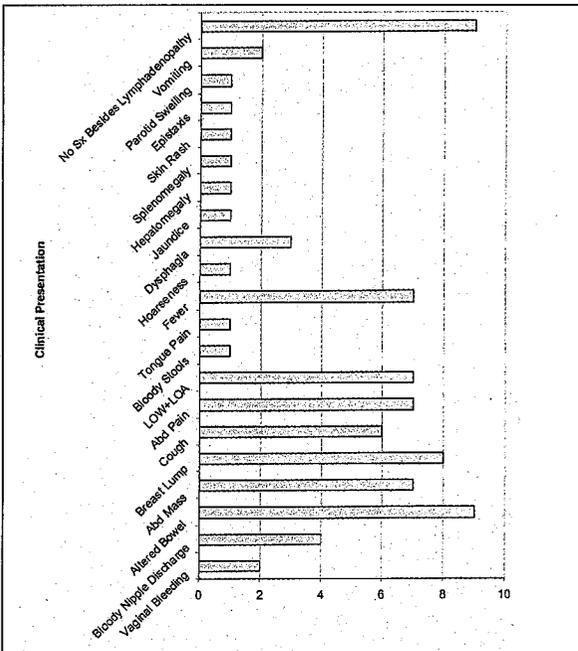


Fig. 14: Clinical presentation adults with chronic non specific lymphadenitis

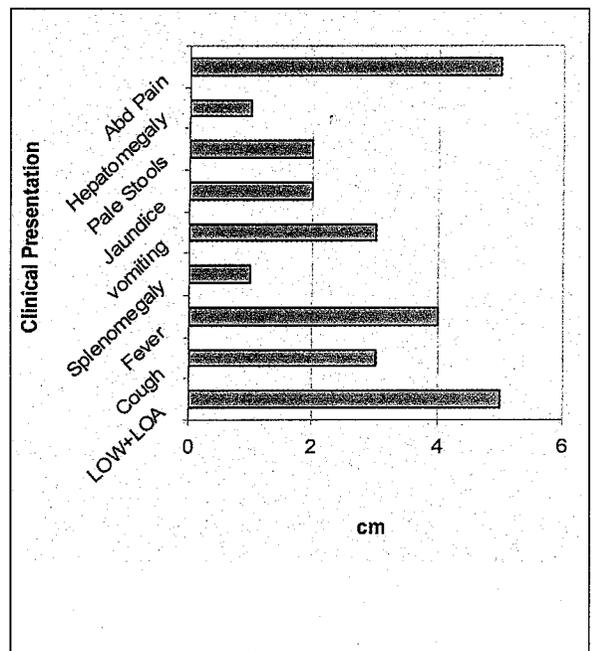


Fig. 15: Clinical presentation in children with chronic non specific lymphadenitis

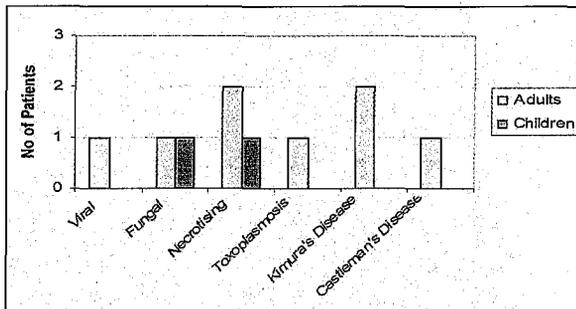


Fig. 16: Type of infective lymphadenitis

Discussion

The prevalence of lymphadenopathy was much higher (87%) in adults than in children (13%) in our analysis while 20% of adults and 4% of children had normal lymph node morphology microscopically. Lymphadenopathy patients have equal gender distribution in adults while there were twice as many male children than the female children (2:1). Patients with Malay ethnicity were found to predominate in both adult and children but Indian children had second highest incident (17%) which was slightly higher than the Chinese children (14%). Though the ethnic frequency was almost fairly distributed among adults and children, the frequency of lymphadenopathy in Chinese adults were twice that of Chinese children. Does this mean higher antigenic exposure in adult Chinese male? This necessitates further investigation. The commonest cause of lymphadenopathy in adults was malignancy (47%). In children it was chronic non specific lymphadenitis (46%) and this correlates with a study done by Knight PJ, 1982⁸.

Majority of Non-Hodgkin's Lymphoma was seen in males (71%) which is similar to the findings of Semenciw R, Mao Y, 2003⁹ and Malays (65%) having T-cell phenotype in 44% and the rest B-cell phenotype in 56%. This incidence of T-cell type is much higher than B-cell reported in most of the studies¹⁰. Majority (53%) of these patients came in with generalized lymphadenopathy. This is probably because patients seek medical attention at a later stage of their illness. Hodgkin's lymphoma occurred more in males than females with a ratio of 2.7: 1 in adults which is similar to the findings of Desforges JF, 1979¹¹. Hodgkin's lymphoma had almost equal ethnic distribution while Non-Hodgkin's lymphoma is predominately found in Malays, 65%. The most common site of swelling is

generalized, 46%. However, the study by Colby TV, 1982¹² shows the common sites of swelling are in the cervical and supraclavicular regions in adults. Mixed cellularity is the most common histological type seen in 46% of adults¹². The majority of adult patients with Hodgkin's and Non-Hodgkin's lymphoma had a lymph node with a size ranging from 2 – 2.5 cm which correlates with the findings of Panglis GA, 1993¹³. Hodgkin's and Non-Hodgkin's lymphoma have a few similar clinical presentation (loss of weight, loss of appetite, fever, cough, hepatomegaly and night sweats)¹⁴ except for the absence of jaundice and splenomegaly in Hodgkin's lymphoma patients and absence of shortness of breath and lethargy in Non-Hodgkin's lymphoma patients, though the numbers are small. Both primary (4 cases = 2 Hodgkin's and 2 Non-Hodgkin's Lymphoma) and secondary (2 cases = undifferentiated carcinoma) malignant lesions of lymph node were also noted in children below 18 years but they were substantially less than in adults. Of the secondary malignancy of the lymph node, adenocarcinoma was prevalent in adult females (81%), Malays (46%) with axillary swelling (66%), highest number of biopsy (71%) with primary from breast (71%), Gastrointestinal tract (48%) and lung (9%) and majority had infiltrating ductal carcinoma (79%). This is because of the high incidence of breast cancer reported in Ipoh General Hospital of which majority have lymphadenopathy and underwent axillary node clearance. Metastatic squamous cell carcinoma were found in adult male (80%), Chinese (40%) with cervical node swelling (67%), primary from lung (46%), tongue (23%) and nasopharyngeal carcinoma (2%).

The clinicopathological comparison between adults and children could not be analysed for primary and secondary malignancy of lymph nodes due to an insignificant number of cases in children. The statistical calculation ($p > 0.05$) further confirms that the comparison is insignificant.

In our study, 100% of children (9) and 96% of adults (25) with granulomatous lymphadenitis had tubercular lesions predominately in males. Tuberculous lymphadenitis predominately seen in Malays adults (62%) and children (45%). In childhood tuberculosis, Orang Asli children (33%) had second highest frequency than the Chinese children (22%). When compared to their very sparse population in the country, this is quite significant. 54% of adults and 18% of children had lymph node size ranging from 1.1-1.5 cm, a common range found in other studies³.

The cervical nodes was the most common site of swelling in adults with tuberculosis³. This was not the finding in children with tuberculosis as they presented with generalized lymphadenopathy (60%) and cervical lymphadenopathy (20%). However, a few studies showed cervical was the commonest site of swelling and generalized lymphadenopathy consists of 10-20% of total cases¹⁵⁻¹⁷. Statistical calculation ($p = 0.03$) further confirms the significance of cervical lymphadenopathy as the commonest site of swelling among adults and generalized lymphadenopathy as the commonest site of swelling among children. Fever, weight loss and loss of appetite were the common clinical presentation of tuberculosis in adults and children.

There were 3 patients with acute non specific lymphadenitis and all were children 18-20. There was a total of 54 adults with chronic non specific lymphadenitis with a male to female ratio of 1:1. Chronic Nonspecific Lymphadenitis were one of the major causes of lymphadenopathy in both adults and children. Most of these patients present with symptoms of respiratory tract infection such as fever, cough and hoarseness, therefore this indicates respiratory tract infection which drain into the cervical region. This is confirmed by significant statistical calculations ($p = 0.04$) which shows that the cervical is the commonest site of swelling seen in both adults and children. The size of the enlarged lymph node were 1.1-1.5cm in adult and children which was a common range found in other studies.³

Adult patients with infective lymphadenitis had viral (1), fungal (Histoplasmosis) (1), necrotizing lymphadenitis (2), toxoplasmosis (1), Kimura's disease (2), Castleman's disease (1) while children had one each of : fungal (Cryptococcus) and necrotizing lymphadenitis.

Several factors must be taken into account when interpreting these results as there were many limitations in this study. Firstly, a valid comparison between adults and children was not possible because the number of cases in children were insufficient. Secondly, the cases that we reviewed were solely from patients who undergone lymph node biopsies, therefore not all causes of lymphadenopathy were considered in this study. Thirdly, we could not draw any conclusions to the ethnic distribution of the various types of the lymphadenopathy since there were not many studies done to compare the distribution of subtypes of lymphadenopathy according to ethnicity in our country. In our study, the Malays were the majority in all types of lymphadenopathy. This correlates to our rough estimation of the population in Ipoh indicating a higher ratio of Malays to Chinese, Indians and others (4.2 : 2.5 : 1 : 0.02 -Department of Statistics Malaysia). Fourthly, the consistency and matting of the lymph nodes could not be included in this study as the clinical reports were incomplete. The fifth limitation was the inability to follow a particular classification for the histological subtypes of Non-Hodgkin's Lymphoma as no standardize classification were used in our patients in Ipoh General Hospital.

Conclusion

In conclusion, there were sufficient etiopathological and clinical features that differentiate between adults and children with lymphadenopathies. The frequency of lymphadenopathy is much higher in adults than in children and most of it is due to secondary carcinomatosis in adults. In children chronic non specific lymphadenitis was the commonest cause of lymphadenopathy followed by tubercular granulomatous lymphadenitis.

1. Goroll AH, May LA, Mulley AG Jr. Primary care medicine: office evaluation and management of the adult patient. 2ed. Philadelphia: Lippincott, 1987.
2. Cynthia SK, Robert EK. Lymphadenopathy in Children. Pediatric Clinic of North America, 1998; 45: 875-88.
3. Robert F. Lymphadenopathy: Differential Diagnosis and Evaluation. American Family Physician, October 15, 1998.
4. Andrew WB, Douglas RS, Lymphadenopathy and Malignancy. American Family Physician, December 1, 2002.

ORIGINAL ARTICLE

5. Libman H. Generalised lymphadenopathy. *J Gen Intern Med* 1987; 2: 48-58.
6. Morland B. Lymphadenopathy. *Arch Dis Child* 1995; 73: 476-9.
7. Fijten GH, Blijham GH. Unexplained lymphadenopathy in family practice. An evaluation of the probability of malignant causes and the effectiveness of physicians' workup. *J Fam Pract* 1988; 27: 373-6.
8. Knight PJ, Mulne AF, Vassy LE. When is lymph node biopsy indicated in children with enlarged peripheral nodes? *Pediatrics* 1982; 69: 391-96.
9. Liu S, Semenciw R, Mao Y. Increasing incidence of non-Hodgkin's lymphoma in Canada, 1970-1996: age-period-cohort analysis. *Hematol Oncol* 2003.
10. Lukes RJ, and Collins RD. Tumours of the Hematopoietic System, Second Series, Fasc 28. Washington, DC: Armed Forces Institute of Pathology, 1992.
11. Desforges JF, Rutherford CJ, Piro A. Hodgkin's Disease. *N Engl J Med* 1979.
12. Colby TV, Hoppe RT, Warnke RA. Hodgkin's Disease: A clinicopathological study of 659 cases. *Cancer* 1982; 49: 1848-58.
13. Pangalis GA, Vassilakopoulos TP, Boussiotis VA, Fessas P. Clinical approach to lymphadenopathy. *Semin Oncol* 1993; 20: 570-82.
14. Kaplan HS. Hodgkin's Disease. Cambridge, MA: Harvard University Press, 1972.
15. Ord RJ, Matz GJ: Tuberculous cervical lymphadenitis. *Arch Otolaryngol*, 1974; 99: 327-29.
16. Black BG, Chapman JS: Cervical adenitis in children due to human and unclassified mycobacteria. *Pediatrics* , 1984; 33: 887-93.
17. Margileth AM, Chandra R, Altman RP: Chronic lymphadenopathy due to mycobacterial infection: Clinical features, diagnosis, histopathology and management. *Am J Dis Child* 1984; 138: 917-22.
18. Linda SN. MD 1; Kamat, Deepak MD, PhD Lymphadenopathy in Children: When and How to Evaluate. *Clinical Pediatrics*. 2004; 43(1): 25-33.
19. Ponder, T. Brent MD a; Smith, Debora CT (ASCP) b; Ramzy, Ibrahim MD c Lymphadenopathy in Children and Adolescents: Role of Fine-Needle Aspiration in Management. *Cancer Detection & Prevention*. 2000; 24(3): 228-33.
20. Herzog LW. Prevalence of lymphadenopathy of the head and neck in infants and children. *Clin Pediatr*. 1983; 22: 485.