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The Pattern of Paediatric Solid Tumours in Lagos

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Summary

Akinsulie AO, Lesi FEA, Onifade EU, Bode CO, Banjo AAF The Pattern of Paediatric Solid Tumours in Lagos *Nigerian Journal of Paediatrics* ***2000; 27:*** **47.** There is a wide variation in the pattern of paediatric solid tumours with differences noted between developed and developing countries and also within geographic regions. A descriptive retrospective study of children under 16 years with solid tumours seen between 1988 and 1998 was undertaken to document the pattern in Lagos at the Lagos University Teaching Hospital (LUTH). A total of 176,990 children less than 16 years of age were seen in the outpatient clinics out of which 440 had sold tumours. A total of 187 children had benign tumours, while 253 children had malignant tumours. This gives a prevalence for paediatric solid tumours of 2.5 per 1000 children under 16 years seen at LUTH. Malignant tumours were commoner among boys while benign tumours were commoner among girls 10 years and above. The common benign tumous included fibroadenoma (53.5 percent), neurofibromat (15.0 percent) and lipoma (13.9 percent). The common malignant tumours were retinoblastoma (20.2 percent), nephroblastoma (18.2 percent) and Burkitt's lymphoma (9.5 percent). The general pattern of solid tumours is in keeping with patterns seen in other developing countries. However, there is a clear difference in the pattern of malignant solid tumours from other developing countries and from an earlier study done in the same centre with the predominance of retinoblastoma and nephroblastoma over lymphomas. Environmental and genetic factors are postulated as likely reasons for the difference. The importance of Cancer Registration is emphasised.

Introduction

IN developing countries, infections still place a huge burden on the health and well being of children. However, with the current drive to improve child survival using the modality of the integrated Management of Childhood illnesses (IMC), the role of non-infectious diseases such as cancers may become more apparent.[1]

It has been estimated that the incidence of paediatric tumours range from 22-36.5/million children in developing countries and between 118.3-138/million children in industrialised countries.[2-5] In some developing countries, it has been documented that cancers account for a small percentage of total paediatric admissions ranging from 0.66 percent to 1.67 percent[6 7] Nevertheless, workers in Nigeria have demonstrated a dramatic increase in the relative frequencies of certain tumours such as intracranial neoplasms, leukemia, renal neoplasms and retinoblastoma.[8] This increasing trend has also been seen with Kaposi's sarcoma among Ugandan children and with certain tumours excluding nephroblastoma and acute lymphoblastic leukaemia among young American children.[9-11]

Regarding the distribution pattern of paediatric tumours, most authors agree that in developing countries lymphomas occur most commonly, whereas in developed countries, leukemias are the commonest tumours[12 13 4] What is not consistent is the pattern of

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occurrence of the lymphomas and other tumours and their sites of presentation. Most African authors agree that Burkitt's lymphoma is the most commonly occurring lymphoma.[6-8 14 15] Nevertheless, the rarity of Burkitt's lymphoma has been well documented among children in Zimbabwe and Malawi.[16 17]

In Nigeria, the overall clinical picture of solid tumours in childhood is not significantly different from that of other developing countries. Several studies agree on the pre-eminence of Burkitt's lymphoma among Nigerian children.[3 13-15 18-20] However, there are differences in the incidences and patterns of presentation. Workers from Ife, Ibadan and Enugu (inland rain forest areas) report very high frequencies of Burkitt's lymphoma (26-76 percent), while those from Lagos and Calabar (coastal rain forest) report lower frequencies (<20 percent).[3 13 14 15 19] It has also been documented that the site of presentation of Burkitt's lymphoma from the Lagos and Enugu areas is facial, while in the Ibadan area it is mainly abdominal.[3 18 19] Various factors are responsible for the pattern of childhood tumours. They include sex, environment, birth weight, age, ethnic group, and the presence of other problems like Human Immune-deficiency Virus infection.[11 12 21-23] There probably is some interaction between these factors, but clearly, the role of genetics and environmental exposure is certain.[13 24 25]

In developing countries some of the problems encountered in managing paediatric tumours include late presentation, high default rate, lack of radiotherapy and the shortage of chemotherapeutic agents.[13] Financial considerations clearly underpin cancer management as the population is largely poor and the treatment long and expensive, oftentimes without an absolute guarantee of a cure. Also, there is a dearth of knowledge on childhood solid tumours which makes the planning of services to meet the needs of these children difficult.

This study aims at documenting the current pattern of paediatric solid tumours in Lagos in order to determine if there has been any change in the past ten years. It is hoped that this will contribute to establishing a database for the registration and tracking of paediatric cancers in Lagos.

Methods

This descriptive retrospective study was done by reviewing the medical records of all children up to 16 years with solid tumours who attended the Lagos University Teaching Hospital between 1988 and 1998. Data retrieved from the records included the age, sex, duration of illness, clinical and pathological diagnosis, treatment given, duration of hospitalisation and outcome. The data was analysed by first determining the distribution of the variables then the appropriate parametric or non-parametric tests were chosen by using the SPSS statistical package. Chi-squared analysis was used to test the degree of association between variables while the Student's 't' test was used to analyse the means obtained. Significance was determined at $p<0.05$.

Results

A total of 440 solid tumours were diagnosed among children aged 16 years and below. Of these, 253 were malignant while 187 were benign. In the period under review, a total of 176,990 children less than 16 years of age were seen in the outpatient clinics and 8,619 of them were admitted. Solid tumours thus accounted for 0.25 percent (2.5 per 1000) of children under 16 years seen and 5.1 percent (51 per 1000) of all admissions (malignant = 3 percent, benign = 2.1 percent) Determining the outcome was possible in 75 children whose records could be traced. Of this number, 61 died, 11 were termed cured and three had relapsed.

The age and sex distribution of the children (Fig 1) show that most children with benign solid tumours were aged 10 years or more with a significantly larger number being girls ($p<0.0001$). On the other hand children with malignant solid tumours, were mostly under five years and did not show any significant sex predilection

Table I shows that fibroadenomas were the most frequently occurring benign tumours (53.5 percent) and were mostly seen among children 10 years and above. Neurofibromatosis was the next frequently occurring tumour (15.0 percent) and was also seen among children 10 years or over. Other benign tumours seen included lipomas (13.9 percent), squamous papilloma (14.3 percent), phyllodes tumour (3.2 percent) enchondroma (2.1 percent), osteoid osteoma (1.6 percent) and myxoma (1.6 percent).

The most frequently occurring malignant solid tumour was retinoblastoma (20.2 percent) followed by nephroblastoma (18.2 percent) (Table II). Other malignant solid tumours seen were Burkitt's lymphoma (9.5 percent), Non-Hodgkin's lymphoma (8.7 percent), osteosarcoma (7.9 percent) intracranial tumours (6.3 percent) rhabdomyosarcoma (5.5 percent) and neuroblastoma (4.7 percent). The age distribution of children with these tumours indicates that retinoblastoma, nephroblastoma and neuroblastoma were primarily problems of children under 5 years of age. On the contrary, rhabdomyosarcoma and os-

Table I

Age Distribution of Benign Solid Tumours

Tumour	*Age (years)*			*Total*
*n(percent)***	*<5 n (percent)**	*5-9 n(percent)**	*≥10 n(percent)**	
Fibroadenoma	1 (1.0)	2 (2.0) 97	(97.0)	100(53.5)
Neurofibroma	5 (17.9)	7 (25.0)	16(57.1)	28(15.0)
Lipoma	12 (46.2)	5 (19.2)	9 (34.6)	26(13.9)
Squamous papilloma	2 (25.0)	2 (25.0)	4 (50.0)	8 (4.3)
Phyllodes Tumour	-	-	6 (100.0)	6 (3.2)
Enchondroma	1 (25.0)	1 (25.0)	2 (50.0)	4 (2.1)
Myxoma	-	-	3 (100.0)	3 (1.6)
Osteoid osteoma	1 (33.3)	-	2 (66.7)	3 (1.6)
Others	3 (33.3)	1 (11.1)	5 (55.6)	9 (4.8)
Total	25 (13.4)	18 (9.6)	144 (77.0)	187 (100)

* = percentage of row total
** = percentage of column total

Table II

Age Distribution of Malignant Solid Tumours

Tumour	*Age (years)*			*Total*
	*<5 n(percent)**	*5 – 9 n(percent)**	*≥10 n(percent)**	*n(percent)***
Reinoblastoma	47 (92.2)	2 (3.9)	2 (3.9)	51(20.2)
Nephroblastoma	27 (58.7)	17 (37.0)	2 (4.3)	46(18.2)
Burkitt's lymphoma	8 (33.3)	10 (41.7)	6 (25.0)	24 (9.5)
Non-Hodgkin's lymphoma	2 (9.1)	15 (68.2)	5 (22.7)	22 (8.7)
Osteosarcoma	1 (5.0)	5 (25.0)	14 (70.0)	20 (7.9)
Intracranial tumours	4 (25.0)	12 (75.0)	-	16 (6.3)
Rhabdomyosarcoma	4 (28.6)	4 (28.6)	6 (42.9)	14 (5.5)
Neuroblastoma	7 (58.3)	3 (25.0)	2 (16.7)	12 (4.7)
Others	13 (27.1)	14 (29.2)	21 (43.7)	48(19.0)
Total	113 (44.6)	82 (32.2)	58 (23.2)	253 (100)

* = percentage of row total
** = percentage of column total

Table III

Frequency of Benign Solid Tumours by Sex

Tumour	Sex		Total	p value
	Male n(percent)	*Female n(percent)*		
Neurofibroma	19 (67.9)	9 (32.1)	28	0.007
Lipoma	15 (57.7)	11 (42.3)	26	NS
Fibroadenoma	2 (2.0)	98 (98.0)	100	<0.0001
Squamous Papilloma	6 (75.0)	2 (25.0)	8	NS
Phyllodes Tumour	-	6 (100.0	6	0.003
Enchondroma	2 (50.0)	2 (50.0)	4	NS
Myxoma	1 (33.3)	2 (66.7)	3	NS
Osteoid osteoma	1 (33.3)	2 (66.7)	3	NS
Others	5 (55.6)	4 (44.4)	9	NS
Total	51 (27.3)	136 (72.7)	187	NS

NS = not significant

Table IV

Frequency of Malignant Solid Tumours by Sex

Tumour	*Sex*		*Total*	*p value*
	Male n (percent)	*Female n (percent)*		
Retinoblastoma	31 (60.8)	20 (39.2)	51	0.03
Nephroblastoma	25 (54.3)	21 (45.7)	46	NS
Burkitt's lymphoma	11 (45.8)	13 (51.2)	24	NS
Non-Hodgkin's lymphoma	13 (59.1)	9 (40.9)	22	NS
Osteosarcoma	10 (50.0)	10 (50.0)	20	NS
Intracranial tumours	12 (75.0)	4 (25.0)	16	0.004
Rhabdomyosarcoma	10 (71.4)	4 (28.6	14	0.02
Neuroblastoma	10 (83.3)	2 (16.7)	12	0.001
Others	27 (56.2)	21 (43.8)	48	NS
Total	149 (58.9)	104 (41.1)	253(100)	<0.0001

NS = not significant

teosarcoma were seen among older children 10 years and above. Burkitt's lymphoma showed a peak age occurrence between 5 years to 9 years.

Table III show the comparative frequencies of solid tumours between the sexes. Among beningn tumours, neurofibroma was commoner among boys (p=0.007) while fibroadenoma was commoner among girls (p<0.0001). Overall, benign tumours were commoner among girls (p<0.0001). Among the malignant tumours (Table IV), those commonly seen among boys were retinoblastoma (p=0.03), intracranial tumours (p=0.004), rhabdomyosarcoma (p=0.02) and neuroblastoma (p=0.001). Overall, malignant solid tumours were commoner among boys (p<0.0001).

Discussion

As we enter the millennium when in Nigeria, we hope to effectively curtail the scourge of infectious diseases, neoplastic diseases may dominate the health needs and medical expenditure of the country. This study shows that solid tumours constitute a small but significant percentage of admissions of children under 16 years at the Lagos University Teaching Hospital (LUTH). The estimated prevalence of 5.1 percent is higher than those obtained from other parts of the African continent and elsewhere in the sub-region including the earlier Lagos report.[3,6,7] The possible reasons for this include the fact the earlier Lagos study was done on patients at autopsy and involved a smaller population. The present study is larger and may be more reliable. Another reason is the possible selection bias of those attending our hospital. The charging of fees for service in Nigerian public hospitals might have resulted in a significant reduction in health service utilization such that only very severe or life-threatening diseases are managed in our tertiary health institutions. The effect of user charges on health facility utilization has been clearly demonstrated in Kenya.[26] The prevalence figure found in this study needs to be interpreted cautiously. Clearly, there is need for more representative data obtained either in the primary care health facilities or in the community from regular health monitoring.

The pattern of solid tumours seen in this study is similar to the pattern for other developing countries. Benign tumours were mainly fibroadenomas which occurred in adolescent girls (p<0.0001), neurofibroma which was commoner among boys (p=0.007) and lipoma. Although these bening neoplasms may not be life-threatening, their potential for disfigurement makes them important reasons for presenta-

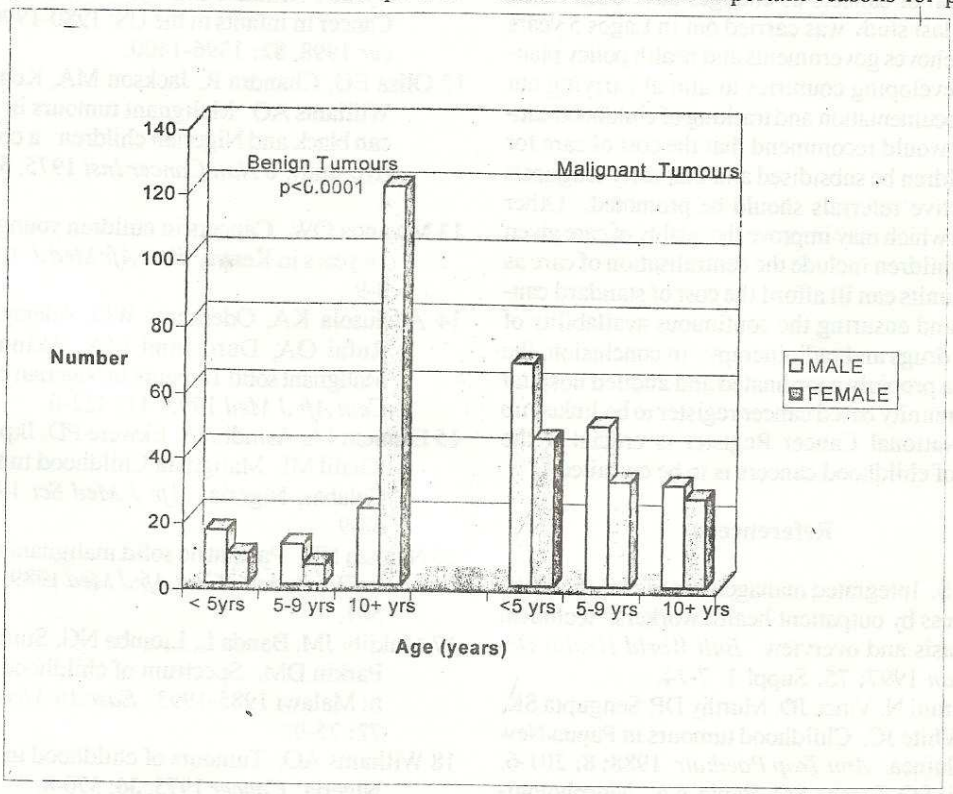

Figure 1: Age and Sex Distribution of Children with Solid tumours

tion to health facilities for cosmetic surgery at a cost, which must be adequately considered, for proper health planning.

With regard to malignant solid tumours, our findings show the predominance of retinoblastoma, followed by nephroblastoma and the lymphomas. While this pattern is not unusual as it has been described in India, it is different from the pattern seen in Popua New Gueinea, Accra, Malawi, Ibadan, Ife, Calabar, Enugu, and in the earlier Lagos reports[2,3,7,8,14,15,17,27] The latter studies all report lymphomas as the commonest malignant solid tumours with a frequency ranging from

32-73 percent.[3,14] Our study confirms that intracranial tumours though not common cannot be considered rare. They were absent from the Ife and Calabar reports though other workers document their occurrence.[3,7,14,15,19] This difference in the pattern of presentation of malignant solid tumours is difficult to explain, the possibility of environmental factors and genetics cannot be disregarded. Ethnic differences have been documented as a possible reason for distribution of some tumours in Kenya, Britain and Namibia.[13,22,27]

From the foregoing, our results underscore the need for regular documentation of the pattern and distribution of cancers as changes have been noted since the last study was carried out in Lagos 5 years ago.[3] It behoves governments and health policy planners in developing countries to aim at carrying out regular documentation and tracking of childhood cancers. We would recommend that the cost of care for these children be subsidised and that early diagnosis and effective referrals should be promoted. Other measures which may improve the quality of care given to these children include the centralisation of care as separate units can ill afford the cost of standard cancer care and ensuring the continuous availability of effective drugs and radiotherapy. In conclusion, the need for a properly coordinated and audited hospital and community based cancer register to be linked up with a National Cancer Register is crucial if the scourge of childhood cancers is to be curtailed.

References

1 Gove S. Integrated management of childhood illness by outpatient health workers: technical basis and overview. *Bull World Health Organ* 1997; **75:** Suppl 1: 7-24.

2 Tefuarani N, Vince JD, Murthy DP, Senguptā SK, White JC. Childhood tumours in Papua-New Guinea. *Ann Trop Paediatr* 1988; **8:** 201-6.

3 Tijanii SO, Elesha SO, Banjo AA. Morphological patterns of Paceddiatric Solid cancer in Lagos, Nigeria. *West Afr J Med* 1995; **14:** 174-80.

4 Stiller CA, Allen MB, Eatock EM. Childhood Cancers in Britain: the National Registry of Childhood Tumours and incidence rates 1978-*1987*. *Eur J Cancer* 1995; **31:** 2028-34.

5 McWhriter WR, Dobson C, Ring I. Child hood cancer incidence in Australia, 1982-1991. *Int J Cancer* 1996; **65:** 34-8.

6 Teka T. Childhood malignancies in an Ethiopian Teaching Hospital. *Ethiop Med J* 1992; **30:** 159-62.

7 Welbeck JE, Hesse AA. Pattern of Childhood Malignancy in Korle Bu Teaching Hospital, Ghana. *West Afr J Med* 1998; **17:** 81-4.

8 Akang EE. Tumours of Childhood in Ibadan, Nigeria (1973-1990). *Paediatr Pathol Lab Med* 1996; **16:** 791-800.

9 Draper GJ, Kroll ME, Stiller CA. Childhood cancer. Cancer Surv 1994;19-20: 493-517.

10 Gurney JG, Davis S, Severson RK, Fang JY, Ross JA, Robison LL. Trends in cancer incidence among children in the US. *Cancer* 1996; **78;** 532-41.

11 Kenney LB, Miller BA, Ries LAG, Nicholson HS, Byrne J Reaman GH. Increased Incidence of Cancer in infants in the US: 1980-1990. *Cancer* 1998; **82:** 1396-1400.

12 Olisa EG, Chandra R, Jackson MA, Kennedy J, Williams AO. Malignant tumours in American black and Nigerian children: a comparative study. *J Natl Cancer Inst* 1975; **55:** 281-4.

13 Mwanda OW. Cancers in children younger than 16 years in Kenya. *East Afr Med J* 1999; **76:** 3-9.

14 Adelusola KA, Odesanmi WO, Adejuyigbe O, Rufai OA, Durosinmi MA, Akinola NO. Malignant solid Tumours in Nigerian children. *Cent Afr J Med* 1995; **41:** 322-6.

15 Ekanem IA, Asindi AA, Ekwere PD, Ikpatt NW, Khalil MI. Malignant Childhood tumours in Calabar. Nigeria. *Afr J Med Sci* 1992; **21**: 63-9.

16 Nkanza NK. Paediatric solid malignant tumours iin Zimbabwe. *Cent Afr J Med* 1989; **35**:496-501.

17 Mukiibi JM, Banda L, Liomba NG, Sungani FC, Parkin DM. Spectrum of childhood cancers in Malawi 1985-1993. *East Afr Med J* 1995; **72:** 25-9.

18 Williams AO. Tumours of childhood in Iibadan, Nigeria. *Cancer* 1975; **36:** 370-8.

19 Obioha FI, Kaine WN, Ikerionwu SE, Obi GO

Ulasi TO. Pattern of childhood malignancy in Eastern Nigeria. *Ann Trop Paediatr* 1989; **9:** 261-5.

20 Aikhionbare HA, Yakubu AM, Afolayan AE. Neuroblastoma, an under-diagnosed tumour: 7-year experience in Zaria. *Ann Trop Paediatr* 1988; **8:** 149-52.

21 Yeazel MW, Ross JA, Buckley JD, Woods WG, Ruccione K, Robison. LL. High birth weight and the risk of specific childhood cancers: a report from the Children's Cancer Group. *J Paediatr* 1997; **131:** 671-7

22 Stiller CA, McKinney PA, Bunch KJ, Bailey CC, Lewis IJ. Childhood cancer and ethnic group in Britain: a United Kingdom Children's Cancer Study Group (UKCCSG) study. *Br J Cancer* 1991; **64**: 543-8.

23 Chitsike I, Siziya S. Seroprevalence of human immunodeficiency virus type 1 infection in childhood malignancy in Zimbabwe. *Cent Afr J Med* 1998; 44: 242-5.

24 Crist WM. Epidemiology. In: Eds. Behrman RE, Kliegman RM, Arvin AM. Neoplastic Diseases and Tumours. Nelson Textbook of Pediatrics 15th Edition. Philadelphia, WB Saunders Co 1996: 1443-4.

25 Shapiro DN. Molecular Pathogenesis. In: Eds Behrman RE, Kliegman RM, Arvin AM. Neoplastic Diseases and Tumours. Nelson Textbook of Pediatrics 15th Edition. Philadelphia, WB Saunders Co 1996: 1444-7

26 Mbugua JK, Bloom GH, Segall MM. Impact of user charges on valnerable groups. *Soc Sci Med* 1995; **41:** 829-35.

27 Pramanik R, Paral CC, Ghosh A. Pattern of solid malignant tumours in children – a ten year study. *J Indian Med Assoc* 1997; **95:** 107-8.

28 Wessels G, Hesseling PB. Unusual distribution of childhood cancer in Namibia. *Pediatr Hematol Oncol* 1996; **13:** 9-20.

Table I

Mean anthropometric measurements in SCA and control subjects

Anthropometric measurement	*Mean (± 1 SD)*		*p value*
	SCA subjects n=119	*Control subjects n=119*	
Height (cm)	102.7 (16.1)	108.6 (17.7)	0.008
Weight (kg)	16.0 (4.6)	18.1 (5.4)	0.002
Left midarm circumference (cm)*	14.1 (1.5)	15.5) (1.2)	0.000001
Left tricipital skinfold thickness (mm)	6.3 (1.8)	6.7 (1.8)	NS
Left subscapular skinflold thickness (mm)	4.9 (1.4)	5.5 (1.7)	NS**

n = 52
** Wilcoxon matched pair test
NS = not significant

patient department of the same hospital within 24 hours of recruiting the SCA subject.

All data including anthropometry (weight, height, mid-upper arm circumference and skinfold thickness) for the subjects and their controls were recorded on a proforma. A beam balance weighing scale, regularly checked for accuracy by the use of a predetermined labelled 10kg weight, was used to weigh all subjects (to the nearest 0.1kg) when scantily dressed. Height (to the nearest 0.1cm) was measured with a stadiometer, the child standing upright with his/her heels, gluteal masses, scapulae, and occiput touching the vertical surface of the instrument. Occasionally, an infantometer was used to measure the recumbent height of children who were yet to stand without support. On such occasions, an assistant helped to place the soles of the feet firmly and perpendicularly on the footboard while the headpiece was used by one of the investigators (G.O.O) to take the reading. The mid-upper arm circumference (to the nearest 0.1 cm) was taken on the left upper arm, exactly midway between the acromion and olecranon processes using a flexible measuring tape regularly checked against a rigid measuring ruler. Skin calipers were used to measure the skinfold thickness to the nearest 0.1mm over the left triceps midway between the acromion and olecranon processes and over the tip of the left scapula. Blood specimen was taken, under very strict guidelines to prevent environmental zinc contamination, for erythrocyte zinc (EZ) concentration estimation by atomic absorption spectrophotometry.[13] Student's t test was used in statistical analysis of collected data, and Wilcoxon matched pair test where data were not normally distributed.

Results

One hundred and nineteen subjects with SCA and an equal number of controls were studied. The subjects and their controls were aged 12 months to 119 months, with a median age of 58 months in both groups. Fifty-seven (47.9 percent) of the subjects were females and 62 (52.1 percent) were males, giving a M:F ratio of 1.1:1.0. Since the subjects with SCA were matched for gender, the same gender distribution was observed in the controls. Of the 119 controls, 98 (82.4 percent) had haemoglobin genotype AA while the remaining 21 (17.6 percent) had genotype AS.

Anthropometric measurements were superior in controls compared to SCA subjects and the difference assumed statistical significance in height, weight and mid-arm circumference (Table I). There was a tendency for the differences in both height and weight to become more pronounced with advancing age as depicted in Figures 1 and 2. The overall mean EZ concentration in SCA subjects was 31.9±9.8 mg/g haemoglobin (range 13.2 – 58.1), and this was significantly smaller than the mean of 42.3±16.2 mg/g haemoglobin (range 5.1 – 99.2) obtained in control subject ($p = 0.0000001$).

As early as the third year of life, control subjects had a statistically significant higher mean EZ concentration than SCA subjects ($p = 0.0109$) with a trend towards statistical significance in the second year of life ($p = 0.077$). At all age intervals, control subjects had higher mean EZ concentration than SCA subjects did. The difference also became more pronounced with advancing age (Fig 3). The mean EZ

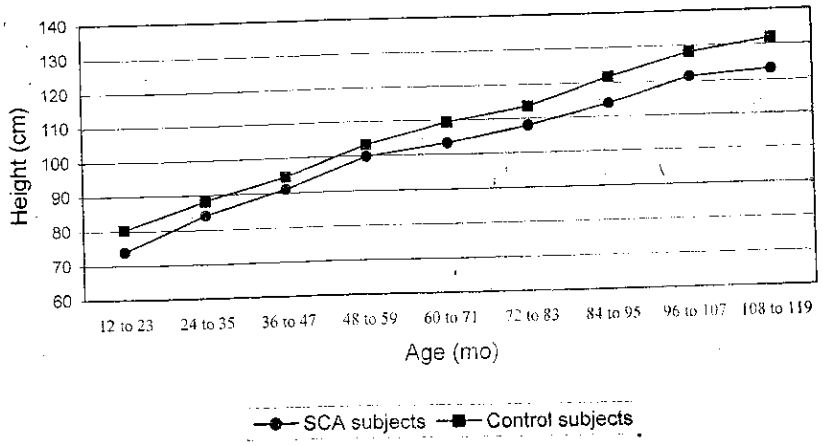

Figure 1. Mean height in SCA and control subjects

concentration in male SCA subjects was 31.9±9.8 mg/g haemoglobin and was lower but not significantly different from the mean value of 32.0±9.8 mg/g haemoglobin obtained for female SCA subjects. The corresponding figures for control males and females are 43.2±14.6 mg/g Hb and 41.4±17.8 mg/g Hb. respectively. The differences were however significant between male control and male SCA subjects ($p = 0.000001$) and between female control and female SCA subjects ($p = 0.000646$).

Among the SCA subjects there was a small but statistically significant positive linear correlation between EZ concentration and height ($r=0.26$, $p=0.0051$; $r^2 = 0.07$). This relationship was stronger among control subjects ($r=0.32$, $p = 0.00036$; $r^2 = 0.10$). Age was also found to be positively and significantly correlated with EZ concentration. In SCA subjects of preschool age the EZ concentration (29.03±9.88 mg/g Hb) was significantly smaller than the concentration in SCA subjects of school age (34.17±0.14 mg/g Hb; $p = 0.00039$). A similar pattern was observed between control subjects of preschool age (38.03±16.11 mg/g Hb) and school age controls (45.69±15.51 mg/g Hb; $p = 0.0098$). Because of these relationships multiple regression analysis of age and height on EZ concentration was performed. The following multiple regression equations were obtained:

a) $Y = 28.71 + 0.01x_1 - 0.04x_2$ (for SCA subjects)
b) $Y = -7.53 - 0.16x_1 + 0.56x_2$ (for control subjects)

Where Y is EZ concentration in mg/g Hb, x_1 is age in months and x_{2is} height in centimetres.

The regression equation for SCA subjects shows that when age is kept constant, EZ concentration (Y) and height (x_2) became inversely related but the partial regression coefficient (-0.04) was not statistically significant ($p = 0.954$). However, when age is kept constant in the control subjects, EZ concentration and height remained positively and significantly correlated (partial regression coefficient = 0.56, $p = 0.0076$).

The pattern of relationship between EZ concentration and weight in both SCA and control subjects

Table II

Linear relationship of anthropometric measurements to erythrocyte zinc SCA and control subjects

Anthropometric measurements	*SCA subjects* (n=119)		*Control subjects* (n=119)	
	r	*p-value*	*r*	*p-value*
Height (cm)	0.26	0.005	0.32	0.0004
Weight (kg)	0.23	0.012	0.30	0.001
Left midarm circumference (cm)*	0.21	0.138	0.22	0.113
Left tricipital skinfold thickness (mm)	-0.12	0.194	-0.10	0.292
Left subscapular skinfold thickness (mm)	-0.15	0.102	-0.09	0.327

*n=52

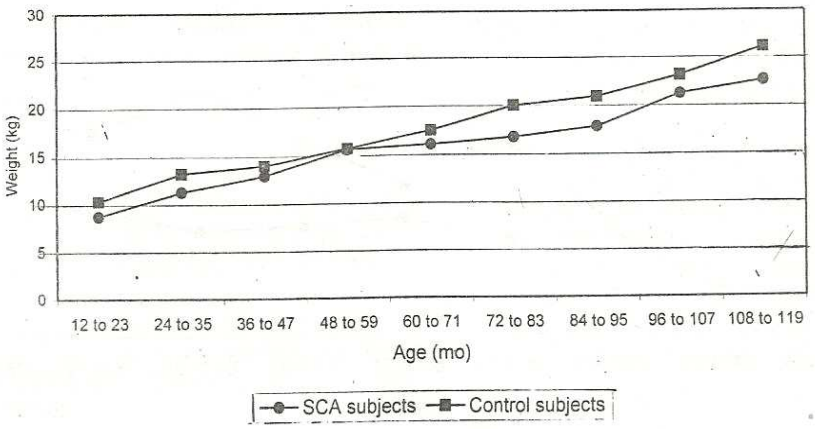

Figure 2. Mean weight in SCA and control subjects

was similar to that observed between EZ concentration and height. When age and weight were regressed on EZ concentration the following multiple regression equations were obtained:

a) $Y = 27.65 + 0.11x_1 - 0.20x_2$ (for SCA subjects)
b) $Y = 26.42 + 0.01x_1 + 0.85x_2$ (for control subjects)

Where Y is EZ concentration (mg/g Hb). x_1 is age in months and x_2 is weight (kg).

None of the partial regression coefficients was statistically significant. This means that with age kept constant, EZ concentration and weight were not significantly correlated, either in the SCA or control subjects. There were no statistically significant linear correlation between EZ concentration and other anthropometric measures in this study, i.e. left tricipital skinfold thickness, left subscapular skinfold thickness, and midarm circumference, in either SCA or control subjects (Table II).

Discussion

This study has demonstrated a significant reduction in height, weight and midarm circumference of sickle cell anaemia subjects when compared to normal control subjects with HbAA and HbAS. The differences in height and weight measurements between SCA and control subjects increased with advancing age. These patterns have been documented in earlier studies.[1,5,14-21] The differences in height and weight measurements were already evident by the second year of life as documented by other workers.[20-22] Unlike what was obtained in earlier studies,[22,23] skinfold thickness (left tricipital and subscapular) did not differ between SCA and control subjects in this study. However, skinfold thickness measurements may not be very reliable for comparing nutritional status given the marked individual differences in the distribution of body fat.[24]

Erythrocyte zinc estimation has not been sufficiently validated to permit its use as a diagnostic criterion for zinc deficiency.[11] However, zinc accumulates slowly in erythrocytes[25,26] and has been said to be reflective of long term zinc status.[27]

Since growth is also a long term physiological process it seems appropriate to study the effect of EZ on growth. In comparison to the control subjects, the SCA subjects in this study were zinc deficient because their mean EZ concentration was significantly lower than the mean for the control subjects. In addition zinc deficiency was detectable by the second year of life but only became statistically significant in the third year. However, because SCA subjects aged 12-23 months already had statistically significant lower anthropometric measurements, the statistically insignificant zinc deficiency noted at this age may actually be clinically significant. The low levels of EZ concentration obtained for SCA subjects in this study are similar to those reported earlier,[8,28] even though the subjects in later studies were either adults or older children.

As has been described earlier[8] age-related increases in EZ concentration were noted in both control and SCA subjects. In this study, SCA and control preschool subjects had significantly smaller EZ concentration than school aged subjects. Also, in each age group, control subjects had greater EZ concentration than SCA subjects with the difference in concentration becoming more pronounced with advancing age. However, it will be difficult to explain the growth retardation noted in the SCA subjects on the basis of zinc deficiency alone as this study has

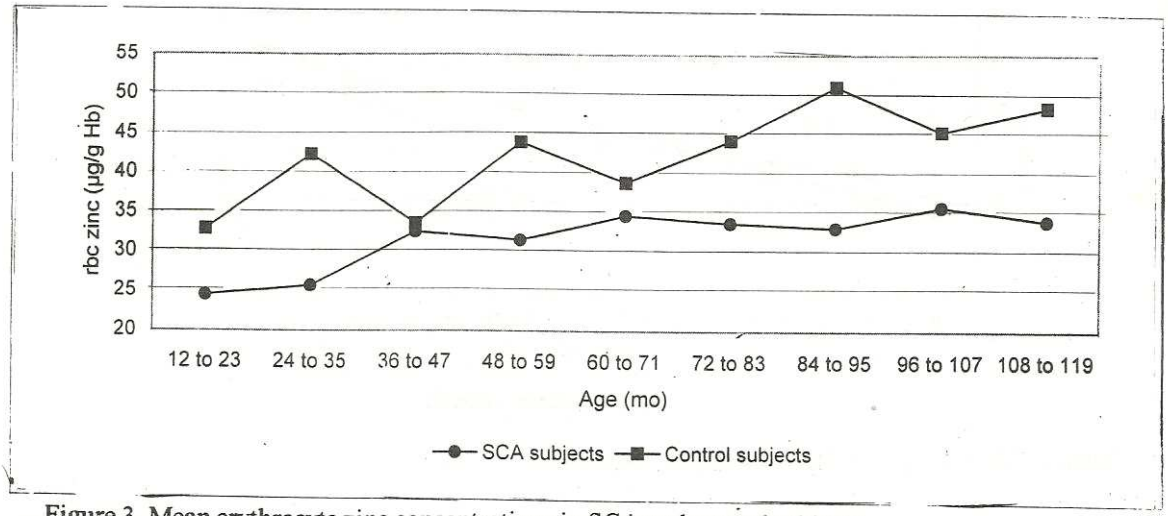

Figure 3. Mean erythrocyte zinc concentrations in SCA and control subjects

not demonstrated any significant linear correlation between EZ concentration and anthropometric measurements in SCA subjects. However, among control subjects there was a significant positive correlation between EZ concentration and height (partial regression coefficient = 0.56, F = 5.091, p = 0.0076). These patterns may suggest an increasingly defective zinc homeostasis in SCA subjects by way of a worsening zincuria or defective intestinal absorption.[8]

Though the significance of lowered EZ concentration in SCA subjects in this study is not clear, it has been shown in earlier studies that zinc supplementation resulted in improved growth patterns,[29-31] increased affinity of the sickle haemoglobin for oxygen without alteration of the Bohr effect,[32] improved androgen levels in patient with testicular failure,[10] healing of ulcers,[9] and reduced incidence of prematurity and improved birthweight.[33] In view of the uncommon occurrence of side effects of zinc supplementation[11] and the need to optimise the prophylactic care of children with SCA, it is recommended that further studies be carried out in Nigerian centres to determine the significance of zinc deficiency in sickle cell anaemia

References

1 Emodi KJ, Kaine WN. Weight, heights and Quetelet's indices of children with sickle cell anaemia. *Nig J Paediatr* 1996;*23:* 37-41.

2 Olarenwaju DM. Complications of sickle cell anaemia – a review. *Nig Med Pract* 1988; **16:** 107-11.

3 Lesi FEA. Anthropometric status of sickle cell anaemia patients in Lagos. *Nig Med J* 1979; *9:* 337-42.

4 Effiong CE. Sickle cell disease in childhood. In: Fleming AF ed. Sickle cell disease: A handbook for the general practitioner. Edinburgh: Churchill Livingstone 1982; **8:** 20.

5 Akinyanju OO. A profile of sickle cell disease in Nigeria. *Annals New York Academy of Sciences* 1989; **565:** 126-36.

6 Chintu C. Complications of sickle cell anaemia. *Postgrad Doctor Afr* 1986; **8:** 20.

7 Daughaday WH. The adenohypophysis. In: William RH ed. Textbook of Endocrinology 5th ed. Philadelphia: WB Saunders 1974; 31-79.

8 Prasad AS, Schoomaker EB, Ortega J et al. Zinc deficiency in sickle cell disease. *Clin Chem* 1975; *21:* 582-7.

9 Serjeant GR, Galloway RE, Gueri MC. Oral zinc sulphate in sickle cell ulcers. *Lancet* 1970; *ii:* 891-3.

10 Prasad AS. Abbasi AA, Rabbani P, DuMouchelle E. Effect of zinc supplementation on serum testosterone level in adult male sickle cell anaemia subjects. *Am J Hematol* 1981; *10:* 119-27.

11 World Health Organization. Trace elements in human nutrition and health. 1996; 72-103.

12 Abshire TC, English JL, Githens JH, Hambidge KM. Zinc status in children and young adults with sickle cell disease. *Am J Dis Child* 1988; **142:** 1356-9.

13 Prasad AS, Oberleas D, Halsted JA. Determination of zinc in biological fluids by atomic absorption spectrophotometry in normal and cirrhotic subjects. *J Lab Clin Med* 1965; **66:** 508-516

14 Platt OS, Rosenstock W, Espeland MA. Influence of sickle cell haemog-lobinopathies on growth and development. N Engl J Med 1984; 311: 7-12.

15 Daeschner CW, Matustik MC, Carpentieri U, Haggard ME. Zinc and growth in patients with sickle cell disease. *J Pediatr* 1981; **88:** 778-80.

16 Kramer MS, Rooks Y, Washington LA, Pearson HA. Pre- and post-natal growth and development in sickle cell anemia. *J Pediatr* 1980; **96:** 857-60.

17 Attah EB. The pathophysiology of sickle cell disease. In: Fleming AF ed.Sickle cell disease. A handbook for the General Clinician.Edinburgh Churchill Livingstone, 1982: **42.**

18 Onwukeme KE. Haematological indices of Nigerians with sickle cell disease. *Nig Med Pract* 1993; *25:* 25-8.

19 Whitten CF. Growth status of children with sickle cell anaemia. *Am J Dis Child* 1961; **102:** 355-64.

20 Finan AC, Elnor MA, Sasanow SR et al. Nutritional factors and growth in children with sickle cell disease. *Am J Dis Child* 1988; **142:** 237-40.

21 Phebus CK, Gloninger MF, Maciak BJ. Growth pattern by age and sex in children with sickle cell disease. *J Pediatr* 1984; **105**: 28-33.

22 Stevens MCG, Hayes RJ, Sergeant GR. Body shape in young children with homozygous sickle cell disease. *Pediatrics* 1983; **71:** 610-4.

23 Kramer MS, Rooks Y, Washington LA, Pearson HA. Pre- and post-natal growth and development in sickle cell anemia. J Pediatr 1980; 96: 857-60

24 James WPT. The assessment of nutritional status. *Medicine Int* 1983; **1:** 663-7.

25 Aammodt RL, Rumble WF, Johnson GS, et al. Zinc metabolism in human after oral and intravenous administration of Zn-69m. *Am J Clin Nutr* 1979; **32:** 559-69.

26 Chvapil M. Effects of zinc on cells and biomembranes. *Med Clin North Am 1976;* **60:** 799-812.

27 Underwood EJ. Trace elements in human and animal nutrition. 4th Ed New York: Academic Press 1977.

28 Prasad AS, Cossack ZT. Zinc supplementation and growth in sickle cell disease. *Ann Intern Med 1984;* **100:** 267-71.

29 Simmer K *et al.* Nutritional rehablitation in Bangladesh – the importance of zinc. *Am J Clin Nutr 1988;* **47:** 1036-40.

30 Walravens PA, Hambidge KM, Koepfer DM. Zinc supplementation in infants with nutritional pattern of failure to thrive: a double-blind, Controlled study. *Pediatrics* 1989; **83**: 532-538.

31 Walravens PA, Krebs NF, Hambidge KM. Linear growth of low income preschool children receiving a zinc supplement. *Am J Clin Nutr* 1983; **38:** 195-201.

32 Hider RC, Ejim L, Taylor PD *et al.* Facilitated uptake of zinc into human erythrocytes. Relevance to the treatment of sickle cell anaemia. *Biochem Pharmacol* 1990; **39**: 1005-12.

33 Cherry FF, Sandstead HH, Rojas P *et al.* Adolescent pregnancy: Associations among body weight, zinc nutriture, and pregnancy outcome. *Am J Clin Nutr* 1989; **50**: 945-54.

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Persistent Peripheral Lymphadenopathy in Childhood in Ibadan

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Summary

Yawe T, Ladipo JK, Thomas JO. Persistent Peripheral Lymphadenopathy in Childhood in Ibadan. *Nigerian Journal of Paediatrics* **2000; 27:70.** Persistent enlarged lymph nodes are common in childhood. This study reviewed the common histopathological diagnosis of biopsied lymph nodes from children seen in the department of Pathology University College Hospital over a 2-year period. The overall diagnostic yield of the biopsied nodes was 70 percent with tuberculosis being the most frequent diagnosis (58.2 percent) especially in enlarged cervical nodes. Reactive hyperplasia (29.9 percent) was more commonly diagnosed in the inguinofemoral nodes.

Introduction

ENLARGED lymph nodes are encountered in many conditions either as a reaction to local or systemic disease, the central focus of which is not necessarily in the lymphoid system. In some instances, enlarged nodes are the initial or most prominent manifestation of the disease and may be the indication for investigations. It has been suggested that biopsy should be done in patients with persistent lymphadenopathy without adequate cause and also in the presence of newly recognized nodes, greater than 1cm diameter or not known to arise from previously recognized cause.[1,2]

Lymphadenopathy in children is common, however, studies on the pattern of diseases in biopsied nodes from children in our environment are relatively scanty in the literature. Earlier reports on biopsied peripheral lymph nodes indicated that the common findings were reactive hyperplasia followed by tuberculosis, lymphoma and secondary tumours.[3] In view of the changing pattern of diseases, this study was undertaken to investigate disease pattern of biopsied lymph nodes specifically in children from Ibadan to update information on current trends and causes of lymph node enlargement in the tropics for practicing clinicians.

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Materials and Methods

The records of all lymph node biopsies seen in the Pathology Department of the University College Hospital, Ibadan, between July 1987 and December 1989, were extracted from the Surgical Pathology Day Registers. Demographic data of the patients and site of biopsy of the nodes were extracted from the patients' records. The slides were reviewed by the pathologist (JOT) and histological diagnosis recorded. Lymph node biopsy data of patients aged 0-14 years were extracted from this and analysed.

Results

During the 30-month period between July 1987 and December 1989, four hundred and thirty-nine (439) peripheral lymph node biopsies were received in the Pathology Department of the University College Hospital. Of these, 134 were from children aged 3-14 years. There was a slight male preponderance with a male to female ratio of 1.5:1. Table I shows the age distribution and frequency of diseases diagnosed whilst Table II shows the range of diagnostic lesions against the anatomical biopsy sites. The most frequently biopsied group was aged 6-10 years (45

percent). The most frequently biopsied nodes were cervical nodes (67 percent of cases). Tuberculosis was the most common diagnosis, which in most instances involved the cervical nodes (61 cases). Reactive hyperplasia, the second most common diagnosis was more likely to be made in biopsied inguinofemoral nodes, as all nodes from the inguinal area showed reactive changes. The main malignancy involving the nodes, were non-Hodgkin's lymphomas with two cases of Burkitt's lymphoma in the peripheral cervical lymph nodes. There were two cases with metastatic nasopharyngeal carcinomas. The overall diagnostic yield of lesions in the biopsied nodes was 70 percent.

Table I

Showing the age Distribution and Frequency of Diseases Diagnosed from Biopsied Node

Age	*Tuberculosis*	*Lymphoma*	*Carcinoma*	*Reactive*	*Others*
0-5	16	0	0	3	0
6-10	39	6	1	23	1
11-14	23	7	1	14	1

Discussion

The enlargement of localized lymph nodes in children in the absence of a primary disease remains a diagnostic and therapeutic dilemma to the clinician. It has been observed that the investigation of such nodes may be difficult for both the patient and the physician, in situations where investigative facilities are limited, unavailable or unaffordable by the patient. Knowledge of the common and likely causes of peripheral lymphadenopathy in childhood would therefore be useful to practicing physician in these situations.

This study, unlike previous reports from Ibadan,[3,4] show that tuberculosis is the commonest cause of biopsied peripheral lymph nodes in children. Similar trends have also been observed in other centres in Nigeria.[5,6] This would indicate that tuberculosis is a significant cause of persistent lymphadenopathy in children and must be excluded in any child with cervical lymph node enlargement and this can easily be achieved by the use of fine needle aspirate. This

Table II

Showing Node Sites Against Frequently Diagnosed Diseases

	Sites of biopsy					
Diseases	*Cervical*	*Axillary*	*Inguinal*	*Unspecified*	*Total*	*percent*
Tuberculosis	61	14	0	3	78	58.2
Lymphoma (NHL Burkitt's)	10	3	0	0	13	9.7
Carcinoma	2	0	0	0	2	1.5
Reactive hyperplasia 1	5	7	10	8	40	29.9
Others	1	0	0	0	1	0.7
	89(67)*	24(18)	10(7)	11(8)	134	100

NHL: Non-Hodgkins lymphoma
* : Figures in parentheses are percentages

site may be affected by spread from tonsillar infection, or by spread from the hilar and mediastinal nodes.

The high prevalence of tuberculosis probably a reflection of the poor economic situation, poor nutrition, overcrowding, ineffective immunization and multiple infections compounded with diminished immunity. The possibility of human immunodeficiency virus infection must also be considered.

Reactive hyperplasia was diagnosed in 29.8 percent of cases, involving mainly the inguinal nodes. The latter finding is probably due to non-specific lymph node changes from repeated trauma or infections resulting from walking barefooted.

Therefore, the inguinal lymph node is not a suitable site for biopsy and histological assessment, especially in the tropics and developing countries. It is important to note, that 25 percent of non-diagnostic reactive nodes may subsequently become diagnosed as or develop lymphoma.[7] Therefore patients with clinical suspicion and a diagnosis of non-specific reactive hyperplasia should be followed up.

The high positive yield of cervical lymph nodes justifies the frequency of biopsies, from that site. Protozoal and filarial infestations were not seen, confirming that these are uncommon causes of periphral lymphadenopathy in Ibadan.

In conclusion, it should be emphasized that the findings in this study reflect the disease pattern in persistent lymph node enlargement, which are likely to be biopsied. However majority of enlarged lymph nodes in children is often in response to detectable local infections and is therefore not biopsied.

References

1 Olafunwa JO, Olomu IN, Onyia MJ. Pri mary peripheral lymphadenopathy in Jos Nigeria. *West Afr J Med* 1992; **11:** 24-8.

2 Slap GB, Brooks SJ, Schwartz S. When to perform biopsy of enlarged peripheral lymph nodes in young patients. *J A M A* 1984; **252:** 1321-6.

3 Attah Ed. B. Peripheral lymph node enlargement in children. *West Afric Envir Child Health* 1974: 184-6.

4 Atta EB. Peripheral lymphadenopathy in Nigeria. *Trop Geogr Med* 1974; **26:** 25660.

5 Adedeji MO, Aghahowa J. The diagnostic value of lymph node biopsies in Benin City, Nigeria. *East Afr Med J* 1989; **66:** 127-33.

6 Ademiluyi SA, Ijaduola GT. Persistent palpable cervical lymph nodes in Nigerian children. *Ann Trop Paediatr* 1988; **8**: 153-6.

7 Sinclair S, Beckman E, Ellma L. Biopsy of enlarged superficial nodes. *J A M A* 1974; **228:** 602-3.

8 Kissare JM, Gerphart GN. Lympadenopathy in childhood: Long term follow up in patients with non-diagnostic lymph nodes. *Hum Path* 1974; **5: 431-9.**