Histopathological Spectrum of Biopsied Sudanese Children: Five Years' Experience: A Retrospective Study

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Abstract
The histopathological spectrum of pediatric surgical specimens from January 2019 to December 2023 was examined in this retrospective study conducted at the Department of Pathology of Kost Teaching Hospital laboratory in White Nile State Sudan. Using age, sex, site and type of biopsy, and histopathological diagnosis as data, the study analyzed 302 histopathological reports of children under the age of 18. The findings indicated a 58. 3% female predominance and the most prevalent age group was 15–18 years old. The gastrointestinal tract was the most commonly affected area with acute appendicitis being the most prevalent condition. The second most common prevalent was breast biopsies which revealed benign fibroadenomas in 92% of cases. Skin biopsies showed hemangiomas as the most prevalent pattern while lymph node biopsies showed 50% reactive lymph node hyperplasia. The most common bone pathology was osteochondroma. The study emphasizes the need for additional characterization of these conditions and offers useful baseline data for future research in pediatric surgical pathology in the area.

Keywords: Histopathological, biopsies, Sudan, pediatrics.

Introduction

Pathology plays a pivotal role in the diagnosis and staging of many diseases which directly influences the plan of patient management. (1, 2) Moreover, pathology now has an important role in the definition of molecular prognostic parameters in cancer which leads to more targeted therapy for cancer patients in developed countries. (3, 4) In Sudan, approximately 15 million of the population are children younger than 18 years. (5) Hence histopathological diagnosis of pediatric surgical biopsies across various organs is very crucial in managing childhood diseases and hence improving patients' outcomes and contributes to health care planning. This is particularly crucial in limited-resource countries like Sudan facing great health challenges, especially in diagnostic tools. To our knowledge, there is a scarcity of published data highlighting the spectrum of pediatric histopathological diagnosis in Sudan. This retrospective study aims to identify the most common histopathological patterns in pediatric surgical biopsies analyzed at Kost Teaching Hospital Laboratory, White Nile State, Sudan during the period from January 2019 to December 2023. By doing so the study can highlight the trend of disease patterns in pediatrics aged 18 years and younger in Sudan and contribute to informed health care planning local authority.

Materials And Methods

This retrospective study was carried out at the Department of Pathology of Kost Teaching Hospital laboratory in White Nile State Sudan and aimed to analyze the spectrum of histopathological diagnosis in children. The records of all the samples diagnosed histopathologically in children less than 18 years of age during five years from January 2019 to December 2023 were retrieved and analyzed. The pathological conditions were analyzed according to age, sex, site and type of biopsy, and histopathological diagnosis. All histopathological specimens were diagnosed on routine hematoxylin and eosin-stained sections. Ethical clearance was approved by the

local Ethical Review Committee (ERC). Data were analyzed using a computer Statistical Package for Social Sciences (SPSS) program version 25.

Results:

We collected about 345 histopathological reports for the biopsied children of which 43 reports were eliminated because of missed data. 302 histopathological reports were enrolled in the study. Female patients were more than (58.3%). The common age group was 15 and < 18 years.

The sociodemographic data of the participants are shown in **Table 1.**

Table 1: sociodemographic data of the participants.

Item	Variables	N (%)
Gender	Males	126(41.7)
	Females	176(58.3)
Age (Years)	< 1 year	10 (3.3)
	1-5 yrs	51 (16.9)
	> 5-10 yrs	54 (17.9)
	> 10-15 yr	84 (27.8)
	> 15 and < 18 yrs	103 (34.1)

Regarding the specimens for histopathology, excisional biopsy was the most common type of biopsy representing 80.1% of all kinds of pediatric biopsies followed by incisional biopsy (9.9%), then endoscopic (4.3%), D & C (2.3%), and cystoscopic biopsy.

Concerning the primary site from which the biopsy was taken, the most common site was gastrointestinal 83 (27.5%) followed by breast 52 (17.2%), then the soft tissues (muscles, subcutaneous tissues, tendons, fibrous tissues) 30 (9.9), skin 29 (9.6%), lymph node 26 (8.6%). The remaining sites include bone, renal, ovarian, uterine, thyroid, testes, tonsils, nasopharynx, salivary glands, ocular, brain, adrenal, and lung **Figure 1.**

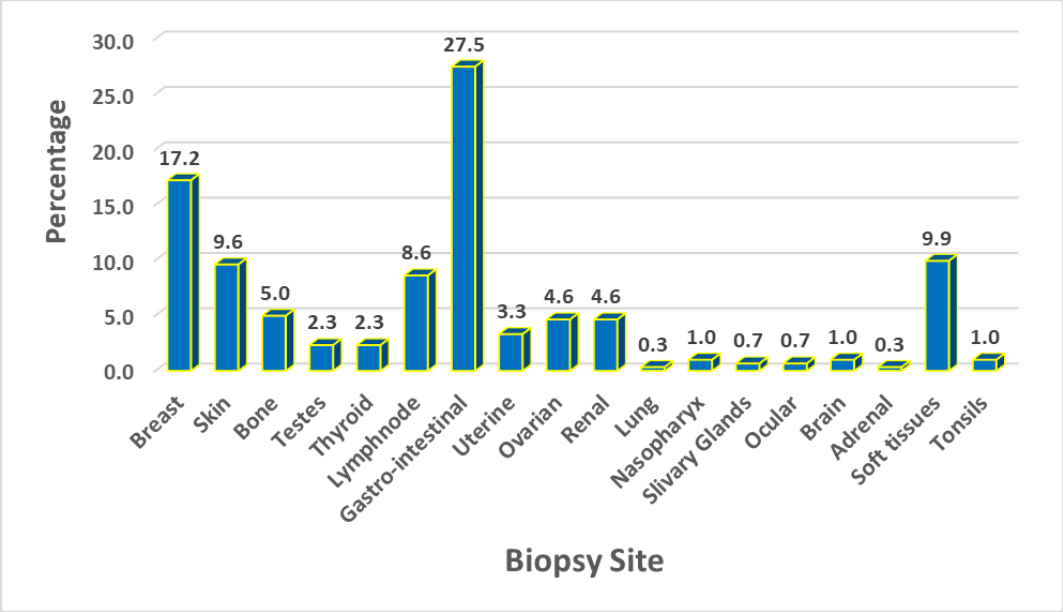

Figure 1: Site of the biopsy.

The results of the 302 histopathological biopsies were classified according to the detected cause into congenital, inflammatory, neoplastic (malignant or benign), others, and normal biopsies. Of the total biopsy results, 108 (35.8%) showed benign neoplastic growth whereas malignant neoplasia was encountered in 21 (7%) specimens. The biopsy results in 95 (31.5%) showed inflammatory causes; in 20 (6.6%), it yielded congenital causes. In 39 (12.9%) of the total biopsies the histopathology showed other causes while 19 (6.3%) of the total specimens showed normal histopathology **Figure 2.**

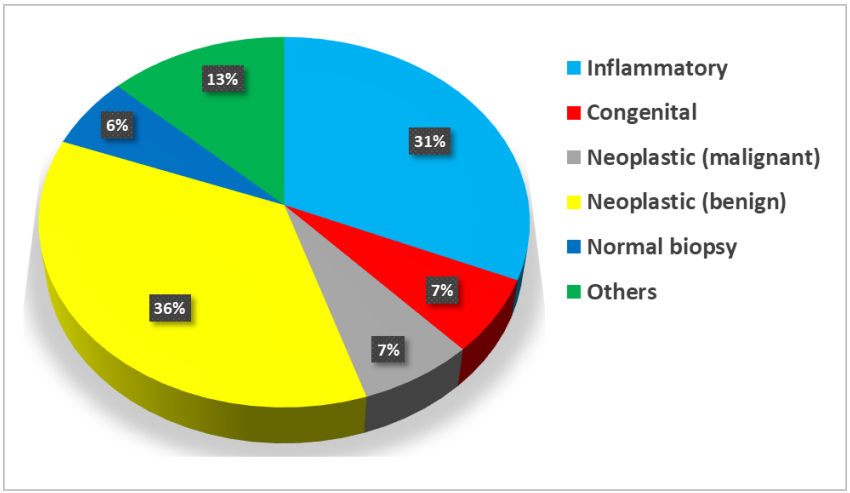

Figure 2: Etiological categories of the diseases.

Regarding the results of the histopathological specimens of the biopsied children, we categorized them according to the site or system of the specimen.
Regarding the gastrointestinal biopsies 20 specimens showed appendicitis (18 acute and 2 chronic), and 17 yielded intestinal polyps (13 juvenile, 1 inflammatory, 1 fibroepithelial, 1 hyperplastic, and 1 retention polyp). In 10 biopsies there was a suspicion of Hirschsprung disease of which 6 cases were negative (ganglion cells were present) and in 4 cases the disease was confirmed by finding absent ganglion cells. There was a suspicion of celiac disease in 7 biopsies of which 6 cases were negative and in only one case the disease was confirmed by finding villous atrophy.
The biopsies taken from the breast were 52 biopsies in 48 (92.3) of these biopsies the histopathology yielded benign fibroadenoma of the breast, and one specimen (1.9%) for each of the following accessory breast tissue, fibrocystic changes of the breast, organized breast abscess, and reactive lymph node hyperplasia.
26 Lymph node biopsies were taken of these 13(50%) showed reactive lymph node hyperplasia, 4 were diagnosed as tuberculous lymphadenitis, 3 biopsies showed Hodgkin lymphoma, 1 biopsy showed metastatic poorly differentiated carcinoma **Figure 3.**

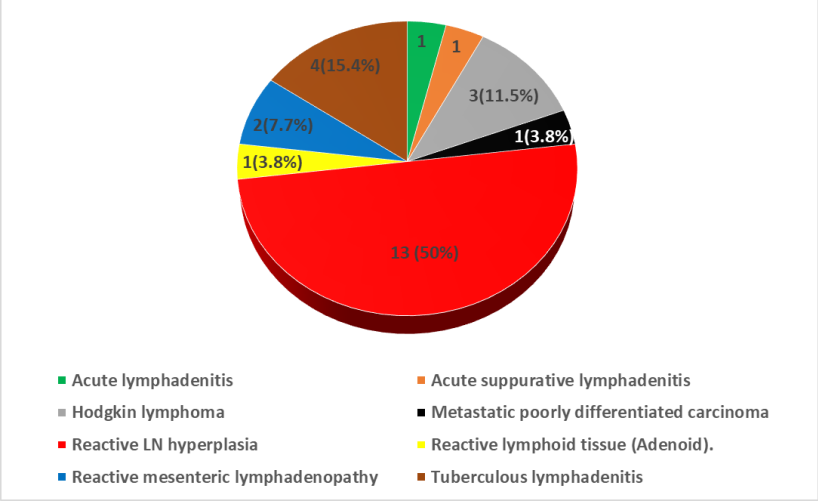

Figure 3: Histopathological pattern of lymph node biopsy.

Regarding the distribution of lymph node involvement, the most common affected group was cervical lymph node 12(46.2%) followed by mesenteric lymphadenopathy 5(19.2%), and two cases (7.7%) for inguinal, supra-clavicular, and preauricular lymphadenopathy and one case (3.8) of submandibular involvement. In two cases the site is undetermined.
The most common histopathological patterns detected in the skin biopsy were hemangiomas 5(17.2%), Fibroma 2(6.9%), psoriasis 2(6.9%), benign skin adnexal tumor 2(6.9), pyogenic granuloma 2(6.9%), non-Hodgkin lymphoma 1(3.4%), and eczema 1(3.4%).

The bone biopsies showed aneurysmal bone cyst 2(13.3%), Chronic osteomyelitis 3(20%), osteochondroma 8(53.3%), osteosarcoma (chondroblastic type) 1(6.7), and femur fracture site 1(6.7%) which was negative for malignancy.
The non-neoplastic conditions have equal sex distribution with a mean age of 13.8± 2.8 years while the benign and malignant neoplastic conditions were common in males with a mean age of 13.8± 3 and 13 years respectively.
While in the soft tissue biopsies, subcutaneous conditions (inflammatory condition, epidermal cyst, and dermoid cysts) were the most prevalent histopathological finding 18(60%), followed by Adipose tissue problems (lipomas and fibro-lipomas) 7(23.3%), then muscle 3(10%) and fibrous tissue problems (Ganglion) 2(6.7%). The non-neoplastic, benign, and malignant neoplastic conditions were common in females with a mean age of 10.1± 5.73, 10.9± 5.13, and 17 years respectively **Table 2.**

Table 2: Age, gender, and pathological categories of bone and soft tissue lesions.

Variable	Category	Gender		Mean Age
		Males	Females	
Bone	Non-neoplastic conditions	2	2	13.8 ± 2.8
	Benign neoplastic	9	1	13.8 ± 3
	Malignant Neoblastic	1	0	13 yrs
Soft tissues	Non-neoplastic	5	7	10.1 ± 5.73
	Benign neoplastic	6	11	10.9 ± 5.13
	Malignant Neoblastic	0	1	17

Malignant tumors in the biopsied children were discovered in 21 specimens the most common tumor was non-Hodgkin lymphoma 4(19.05%) followed by Hodgkin lymphoma and nephroblastoma 3(14.3%), then granulosa cell tumor and poorly metastatic differentiated carcinoma 2(9.52%) **Figure 4.** At the same time, the most common benign tumor was osteochondroma which was reported in 8 specimens.

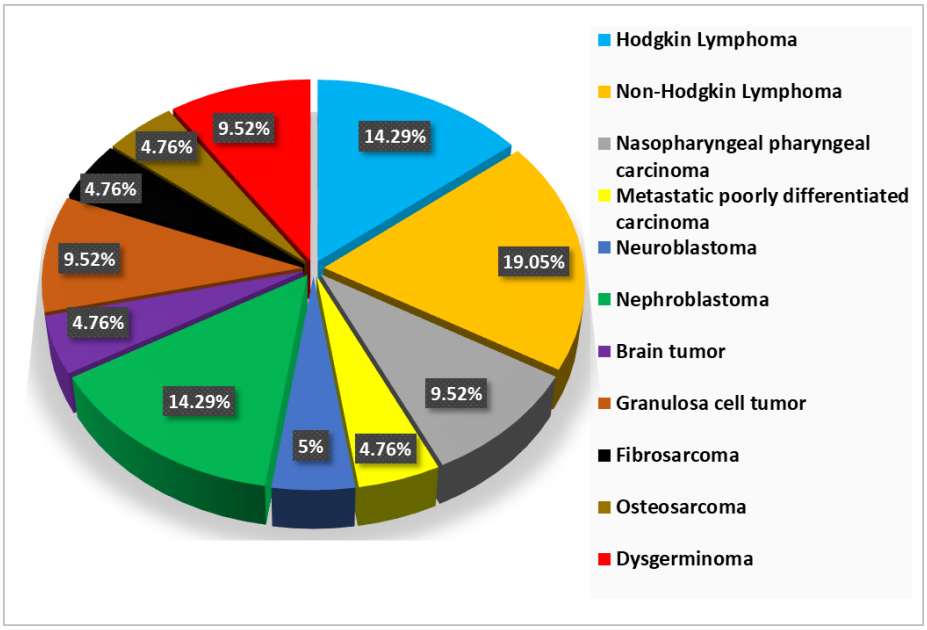

Figure 4: Histopathological spectrum of Childhood malignant tumors.

The histopathological spectrum of the fourteen taken renal biopsies showed urinary schistosomiasis in 7 cases (50%), nephroblastoma in 3 cases (21.4%), chronic cystitis in 2 cases (14.3%), and one case (7.1%) for each of chronic pyelonephritis and multicystic renal dysplasia.
There is a difference between males and females in the method of taking the biopsy this difference is statistically significant (P-value = 0.002) as it is for the site of the site biopsy (involved system) (P-value < 0.001) **Table 3.**

Table 3: Association between the patient age and gender and the type, and site of the biopsy.

Factor	Response	Gender		P-value	Age					P- value
		Males	Female		< 1yr	1-5 yrs	>5-10 yrs	>10-15 yrs	>15-18 yrs	
Type of the biopsy	Excisional	96	146	**0.002**	5	39	47	62	89	**0.003**
	Incisional	17	13		5	11	2	9	3	
	Endoscopic	5	8		0	1	3	5	4	
	Cystoscopic	8	2		0	0	2	6	2	
	D & C	0	7		0	0	0	2	5	
Site of the biopsy	GIT	48	34	< 0.001	6	23	20	20	13	< 0.001
	Breast	0	52		0	0	0	12	40	
	Lymph node	16	10		1	4	11	8	3	
	Renal	10	4		0	4	3	5	2	
	Bone	12	3		0	0	1	9	5	
	Skin	13	16		2	4	4	7	9	
	Soft tissues	11	19		1	3	4	9	6	

The mean age and age group for the most common diseases for each system are shown in **Table 4.**

Table 4: Mean age and age group for the most common diseases.

Biopsy Site	Underlying histopathology	Frequency	The most affected age group	Mean age (In years) ±SD
Lymph node	Reactive LN hyperplasia	13	5-10 years	9.2 ± 4.36
	Tuberculous lymphadenitis	4	10-15 years	
GIT	Acute appendicitis	20	10-15 years	8.8 ± 5.57
	Juvenile polyp	17	1-5 years	
Breast	Fibroadenoma	48	15-18 years	16.6 ± 1.56
	Fibrocystic changes	1	15-18 years	
Skin	Hemangioma	5	1-5 years	10.98 ± 5.61
	Psoriasis	2	10-15 years	
Soft tissues	Lipoma	5	10-15 years	10.8 ± 5.33
	Epidermal cyst	3	5-10 years	
Malignant Tumors	Non-Hodgkin Lymphoma	5	5-10 years	10.3 ± 4.87
	Nephroblastoma	3	1-5 years	
Bone	Osteochondroma	8	15-18 years	13.7 ± 2.76
	Chronic osteomyelitis	3	10-15 years	
Renal	Urinary Schistosomiasis	7	10-15 years	9.9 ± 5.54
	Nephroblastoma	3	1-5 years	

Discussion:

Of the 302 histopathological reports analyzed the findings reveal that most of the patients were female (58.3%), and the most common age group was between 15 and 18 years. Our result is not aligned with a study conducted by Shah, N., et al and Seema Bijjaragi et al. who observed a higher proportion of pediatric male patients, this discrepancy might result from the fact that in the adolescent period, which is not involved in their study, girls may be more likely to undergo biopsies due to concerns about breast masses, which are common in this age group. (6, 7)

The gastrointestinal tract emerged as the most frequently affected area. Acute appendicitis is the most common surgical emergency in children, and the number of acute situations in our study (18 out of 20) aligns with results from the research done by Bhangu et al. (2015), which shows that most appendicitis in children is acute, with chronic appendicitis being uncommon. (8) Chronic appendicitis, though less common, is frequently missed because its symptoms are mild and take a long time to appear.

Regarding juvenile polyps, our study revealed a dominance of juvenile polyps (13 out of 17), consistent with findings from the work conducted by Thakkar et al. which also reports that juvenile polyps are the most frequently encountered type in pediatric populations. (9) These polyps are generally benign and have a good

prognosis following polypectomy. The presence of other types of polyps such as inflammatory, fibroepithelial, hyperplastic, and retention polyps is less common but documented in the literature. (10)

Hirschsprung disease (HD) is considered a relatively uncommon disorder, occurring in approximately 1 in every 5,000 live births, as indicated by Amiel et al. (11) It is diagnosed histologically by an absence of ganglion cells in the affected area. In our study, 4 out of 10 cases suspected of having HD were confirmed. The rate of confirmed cases in our research aligns with findings reported by Vervloet et al. which frequently report that not all clinically suspected cases are histologically validated. (12) This underscores the difficulties associated with clinical diagnosis, as symptoms may overlap with other conditions that lead to chronic constipation or bowel obstruction in pediatric patients.

The prevalence of celiac disease varies across different populations, with an estimated global impact of approximately 1% of individuals. In pediatric cases, diagnosis is generally established by villous atrophy in small bowel biopsies, as demonstrated in research conducted by Hill et al. (13) The observation of 1 confirmed case among 7 suspected instances underscores the critical role of histopathological evaluation, given that clinical manifestations alone may not provide a definitive diagnosis. The relatively low rate of positive diagnoses for celiac disease in our study aligns with findings from other investigations, which indicate that numerous children suspected of having the condition do not fulfill the histological requirements for a diagnosis. This discrepancy may arise from several factors, including poor sampling and processing, unexpired pathologist, non-celiac gluten sensitivity, alternative gastrointestinal disorders that present similarly to celiac disease, or the existence of mild or early-stage disease that has not yet led to significant villous atrophy (14, 15)

The breast emerges as the second most prevalent site for pediatric biopsies, accounting for 17.2%, which is a significant observation. In our investigation, 48 of 52 biopsies (92.3%) demonstrated histopathological characteristics indicative of benign fibroadenoma. This is comparable to the current literature. Nwafor et al. note that most neoplastic breast lesions in children and adolescents are benign, with fibroadenomas representing the most common type, comprising 80-95% of such cases. (16)

Concerning lymph node biopsies, our study analyzed 27 samples from pediatric patients, revealing a higher incidence in males, particularly within the age group of 5 to 10 years. The histopathological results indicated that 50% of the cases exhibited reactive lymph node hyperplasia, while 15% showed tuberculous lymphadenitis, 11.5% were diagnosed with Hodgkin lymphoma, and 3.8% presented with metastatic poorly differentiated carcinoma. Demographic data revealed a male predominance of 61.5%. A comparable study conducted in India on the clinicopathological characteristics of lymphadenopathy also reported a male predominance, with a male-to-female ratio of 1.67:1. (17)

The ages of the patients varied according to the underlying causes, with a notable trend towards younger ages (mean 6.5 years ± 3.8 years) in cases attributed to benign etiologies. (18)

The observation that 50% (13 cases) of the biopsies revealed reactive lymph node hyperplasia, followed by tuberculous lymphadenitis in 15% (4 cases), is consistent with findings from other pediatric studies. For example, Akhter et al. reported that among 160 pediatric lymph node biopsies, 86.9% (139 cases) exhibited reactive hyperplasia, while 11% (7 cases) were diagnosed with tuberculous lymphadenitis. (18) This slight discrepancy may be explained by the larger sample size in the comparative study.

In our investigation concerning skin biopsies, we observed a marginally higher representation of females (61.5%). The predominant age group affected was school-aged children (5-15 years), who constituted 42.3% of the cases. Similar findings were reported in Indian studies conducted by Solanki A. et al. and Ozkanli et al. which analyzed pediatric skin biopsies in outpatient settings, revealing comparable gender and age distributions. (19, 20) Whereas a study by Bendale, et al showed a higher male preponderance (21). This discrepancy may be attributed to variations in the conditions examined or demographic differences within the study populations.

The study results indicated that hemangiomas were the most common histopathological pattern detected in skin biopsies, accounting for 20% of the cases. This was followed by fibromas, psoriasis, and benign skin adnexal tumors, constituting 8% of the cases. Less common were non-Hodgkin lymphoma and eczema, each making up 4% of the cases. This is consistent with findings from a study by Theilaer et al. in Swess Pediatric Skin Center where of 506 patients examined, 401 patients (79%) were given a diagnosis in the spectrum of benign tumors, hamartomas, or cysts. Followed by inflammatory dermatoses found in 93 (18%) cases. In 12 (2%) tissue samples deriving from 4 patients, a malignant tumor was detected. (22)

Our findings contrast with numerous studies in the literature that report a predominance of infectious and non-infectious dermatoses as the most common conditions encountered.(19,20,21) This discrepancy is related to the treatment of many infectious and non-infectious skin diseases in the study area based on clinical evaluation rather than biopsy. Furthermore, the specialized dermatopathology laboratory is increasingly distancing itself from clinical environments. Differences in sample size and geographical location might also contribute to the discrepancy.

The distribution of bone pathologies in our study, with osteochondroma being the most prevalent, aligns well with established patterns in orthopedic pathology. Studies by Schajowicz et al. report similar prevalence rates, highlighting osteochondroma as the most frequent benign bone lesion, often found incidentally during imaging for other conditions. (23)

Focusing on malignant neoplasm our study found that lymphoma was the most common malignant tumor accounting for 34.3 % of malignant cases, a result that is to some extent comparable to a local study conducted in Gazira which reported 26%, representing the second common type after hematological malignancies which is not considered in our study. (24) The rest of the cancer encountered is not comparable with other works because of the small number of cases in our study.

Limitations:

Despite a thorough search, we were unable to locate similar studies related to the histopathological spectrum of pediatric surgical specimens both locally and globally, preventing authors from discussing the variations in regional and global similar situations.

Conclusion:

The distinctiveness of the current investigation into pediatric surgical pathology cases is underscored by the inability to identify similar reports despite a comprehensive online literature review. Neoplastic conditions account for over 50% of the cases, with lymphoma being the most prevalent malignancy observed. The gastrointestinal tract has been identified as the area most frequently affected, with acute appendicitis recognized as the most common gastrointestinal condition. In adolescent females, fibroadenomas represent the most prevalent breast pathology. Notably, half of the lymph node biopsies indicated reactive lymph node hyperplasia, followed by cases of tuberculous lymphadenitis. This study will provide foundational data for future research aimed at further characterization.

Authors´ contribution to the research

1. **Moataz M Alhassan:** Preparation of the research proposal, writing and revision of the manuscript.
2. **Elfatih Mirghani Mohammed Salih**: Study design, data entry and analysis, writing and revision of the manuscript.
3. **Elsadig Ahmed Adam Mohammed:** Preparation of the research proposal, data acquisition, and revision of the manuscript.
4. **Rabei M. Elbadry:** Preparation of the research proposal, and revision of the final manuscript.
5. **Mohammed Eltoum Hamed Azoz:** Preparation of the research proposal, data acquisition, and revision of the final manuscript.
6. **Khalid Al Awad A. Mohammed:** Preparation of the research proposal, writing and revision of the manuscript.
7. **Mohammed Yousof Bakhiet:** Preparation of the research proposal, and revision of the final manuscript.
8. **Omer M. Aburaida:** Preparation of the research proposal, and revision of the final manuscript.

- All authors read and approved the final manuscript.

Conflict of interest: The authors declare that there is no conflict of interest.

Funding: This study received no external funding.

Data and material Availability: All data associated with this study are present in the paper.

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