Role of Fine Needle Aspiration Cytology in Diagnosis of Children and Adolescents' Lesions.

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Abstract
Introduction:
Fine Needle Aspiration Cytology (FNAC) is an increasingly used important investigation tool for assessing childhood mass lesions. It has valuable diagnostic efficacy and utility in diagnosing childhood lesions.
Methodology:
This retrospective study was carried out over four years from January 2018 to December 2022 at the Histopathology and cytology Department of the Health Insurance Laboratory in Kosti - Sudan, including all cytologically evaluated pediatrics samples referred to the laboratory during the study period. Details about the patients' demographic characteristics, the site of aspirations, and their cytopathological diagnoses were obtained from the laboratory's records.
Results: A total of 138 specimens were included in the study. Lymph nodes (LN) were the most common biopsy site (50%) followed by the breast (20.3%). The most involved LN group was the cervical (81%). Non-neoplastic lesions were the most common underlying cytology (73.9%) with the predominance of inflammatory lesions (78.4%). The neoplastic lesions constituted (26.1%) of the total specimens of which 28(20.3%) were benign lesions. whereas malignant neoplasia was encountered in 8(5.8%) specimens.
Conclusion: Lymph nodes FNA were the most encountered specimens with cervical LN predominance. Fortunately, three-quarters of the specimens showed non-neoplastic lesions, whereas one-quarter represented neoplastic lesions with a predominance of benign neoplasm.

Keywords: Lesions, cytology, breast, neoplastic, specimen, inflammatory, lymph nodes.

Introduction:
Fine Needle Aspiration Cytology (FNAC) is a technique used to collect cellular materials for cytological examination and diagnosis, using a “fine” needle to ensure patient comfort. The needle is thinner than that used to withdraw blood, usually, a 21-gauge or even smaller is used with a 5, 10, or 20 ml syringe. Biopsies in children and teens have to be performed under attentive sedation or distraction, using ultrasound guidance to maximize the accurate placing of the needle within the target organ [1, 2]. It is usually used to collect samples from difficultly accessed organs or tissues such as the liver, kidney, or lung [3].
FNAC is an easy and safe investigation tool with minimal discomfort to the patient making it the preferred initial investigatory tool [4].
Fine Needle Aspiration Cytology (FNAC) is a widely used important investigation tool for assessing childhood mass lesions. Data proved its valuable diagnostic efficacy and utility in childhood head and neck lesions [5]. FNAC plays a central role in the early diagnosis of childhood tumors, whether malignant or benign tumors, such as nephroblastoma, hematolymphoid neoplasms, and small round-cell tumors [6]. The increasing incidence of pediatric thyroid neoplasm has intensified the use of FNAC in diagnosing malignant variants, especially papillary thyroid cancer, as well as selecting the proper surgical and medical plan of management [7]. Moreover, FNAC has a high specificity and sensitivity in picking up childhood tumors, helping in the accurate recognition of rare childhood tumors through cytomorphologic characteristics and clinical and radiological correlation [8].
Besides tumors, FNAC is used to diagnose many conditions such as assessment of the cause of lymphadenopathy being reactive, inflammatory, metastatic, and lymphoproliferative [9], reliable and accurate

evaluation of breast lumps [10], thyroid nodules [11], bone lesions [12], skin lesions [13], renal and adrenal masses[14, 15], and for pleural effusion [16]. To our knowledge there is no similar study exists on this subject in our country concerning pediatric general cytopathology, in addition, related data are scarce in the literature regarding the same issue under study. This study aims to detect the cytopathological spectrum of fine needle aspiration biopsies in Sudanese children who undergo a biopsy procedure over four years.

Methodology: This retrospective study was carried out over four years from January 2018 to December 2022 at the Histopathology and cytology Department of the Health Insurance Laboratory in Kosti - Sudan, including all cytologically evaluated pediatrics samples referred to the laboratory during the study period. Details about the patients' demographic characteristics, the site of aspirations, and their cytopathological diagnoses were obtained from the laboratory's records.

Results:
We collected about 150 Fine Needle Aspiration results for the biopsied children of which 12 reports were discarded because they contain missed data. 138 cytology reports were included in the study. Female patients were more than males 83(60.1%). The common age group was 10 and < 15 years representing 47(34.1%). The sociodemographic data of the participants are shown in **Table 1.**

Item	Variables	N (%)
Gender	Males	55(39.9)
	Females	83(60.1)
Age (Years)	< 1 year	5(3.6)
	1-5 yrs	18 (13)
	> 5-10 yrs	24 (17.4)
	> 10-15 yr	47 (34.1)
	> 15 and < 18 yrs	44 (31.9)

Table 1: The sociodemographic data of the participants

The most common site primary site from which the biopsy was taken was lymph node 69 (50%) followed by the breast 28 (20.3%), then the subcutaneous tissue 13 (9.4%), thyroid 10 (7.2%), skin 4 (2.9%), and the pleura 4 (2.9%). The remaining sites include bone, renal, GIT, adrenal gland, tendon sheath, and ascitic fluid.
The results of the 138 FNAC specimens were classified according to the underlying cytology into non-neoplastic 102(73.9%) and neoplastic 36(26.1%). The non-neoplastic specimens were divided according to their etiology into inflammatory 80(58%), congenital 2(1.4%), others 18(13%), and normal biopsy 2(1.4%). Of the neoplastic lesions, 28(20.3%) showed benign neoplastic growth whereas malignant neoplasia was encountered in 8(5.8%) specimens **Figure 1**.

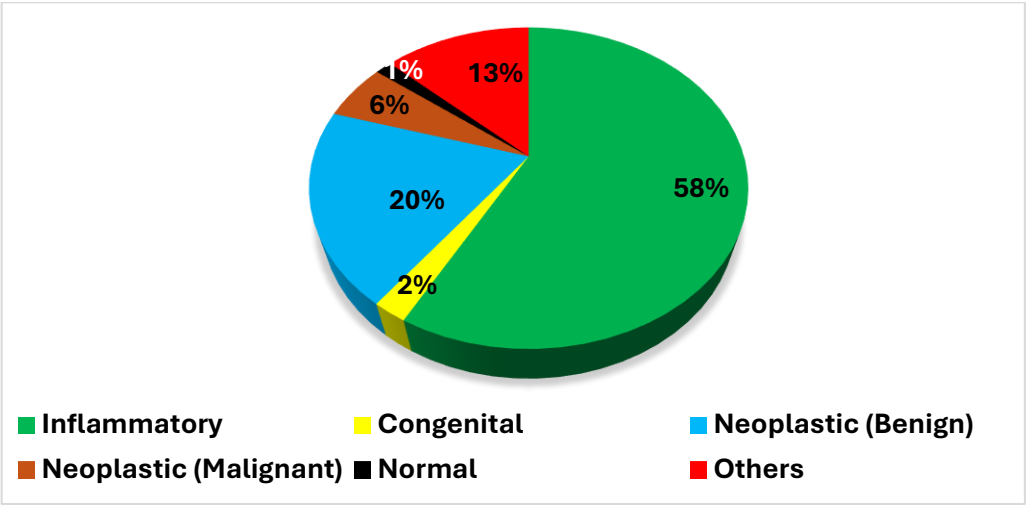

Figure 1: Underlying etiology of specimens' result.

For inventory and regulatory purposes, we categorized the results of FNAC in the biopsied children, according to the site or system of the specimen.

69 lymph node biopsies were taken of these 42(60.9%) showed reactive lymph node hyperplasia, 7(20.6%) were diagnosed as tuberculous lymphadenitis, 13(18.8%) chronic granulomatous lymphadenitis, 3 biopsies (4.3%) showed Hodgkin lymphoma, 3(4.3%) biopsy showed acute suppurative lymphadenitis, and 1(1.4%) metastatic cancer (Positive malignant cells).
The most involved lymph node group was cervical 56(81.2%) followed by submandibular 6(8.7%), axillary 3(4.3%), generalized lymphadenopathy 2(2.9%), and one case for each of periauricular and supraclavicular 1(1.4%) **Figure 2.**

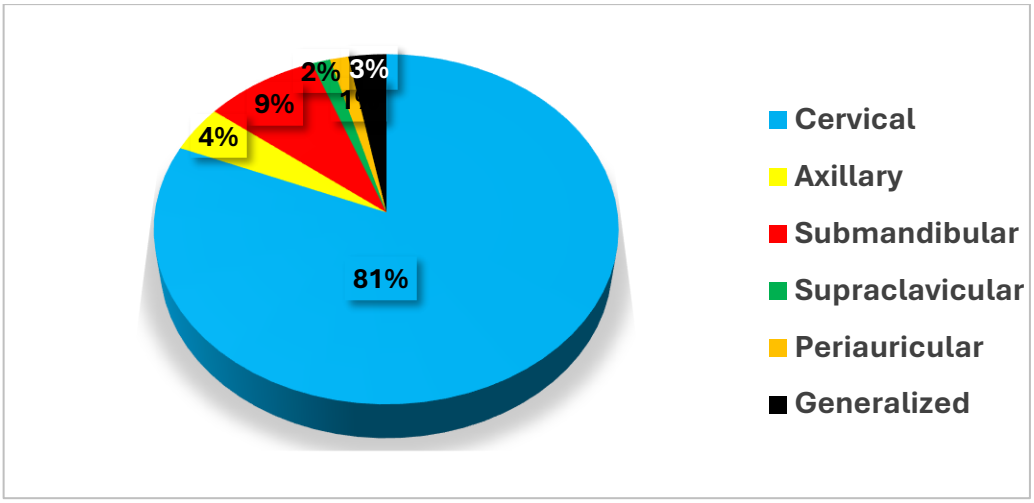

Figure 2: Lymph node group involvement.

Twenty-eight biopsies were taken from the breast, 26(92.9%) were females and two cases (7.1%) were males. The cytology in 20 (71.4%) biopsies yielded benign fibroadenoma of the breast, 3(10.7%) cases showed fibrocystic changes of the breast, and one case (3,6%) was breast abscess. The two male cases revealed gynecomastia and in two cases the cytology showed normal unremarkable breast tissue.
The most common cytopathological patterns detected in the skin biopsy were fibroma (50%) followed by Hemangioma and Infected retention cyst (25%) for each of them. In the soft subcutaneous tissue biopsies, eumycetoma was the most prevalent cytopathological finding 3(21.4%) followed by hemorrhagic cyst, infected cyst, and lipoma 14.3% for each.
The cytopathological spectrum of the ten thyroid-taken biopsies showed 5(50%) colloid goiter, 3(30%) colloid cysts, and 1(10%) for each of chronic suppurative infection and hemorrhagic cyst.
Six fluid aspirates were taken for cytology, four from the pleura and two from ascitic fluid. All pleural fluid aspiration cytology yielded an inflammatory pleural effusion. Whereas in the two ascitic fluid samples, the cause of ascites was found to be metastatic cancer (Positive malignant cells).
Three biopsies were extracted from swelling of the tendon sheath, and all of them yielded ganglion. One biopsy was taken from the bone, vertebrae, and adrenal gland in which the cytology showed eumycetoma, retroperitoneal mass/ small round blue cells (Ewing sarcoma), and neuroblastoma respectively **Table 2.**

Table 2: Cytological spectrum of different tissue biopsies

Biopsy site	Cytopathological spectrum	No	%
Skin	Fibroma	2	50%
	Hemangioma	1	25%
	Infected retention cyst	1	25%
Soft subcutaneous tissues	Acute suppurative infection (abscess)	1	7.1%
	Cystic hygroma	1	7.1%
	Dermoid cyst	1	7.1%
	Eumycetoma	3	21.4%
	Hemorrhagic cyst	2	14.3%
	Infected cyst	2	14.3%
	Lipoma	2	14.3%
	Sebaceous cyst	1	7.1%
	Ganglion	1	7.1%
	Chronic suppurative infection	1	10%

Thyroid	Colloid cyst	3	30%
	Colloid goiter	5	50%
	Hemorrhagic cyst	1	10%
GIT	Tuberculous mesenteric lymphadenitis	1	50%
	Ranula	1	50%
Fluid cytology (Ascites and Pleural effusion)	Metastatic peritoneal cancer (Positive malignant cells)	2	33.3%
	Inflammatory pleural effusion	4	66.7%
Bone and Vertebrae	Eumycetoma	1	50%
	Retroperitoneal mass/ small round blue cells (Ewing sarcoma)	1	50%
Adrenal gland	Neuroblastoma	1	100%

In 8 biopsies, the cytology was reported as malignant tumors, 3 specimens (37.5%) showed Hodgkin lymphoma, all of which presented with lymphadenopathy (two cases cervical and one generalized lymphadenopathy). Three cases (37.5%) were metastatic cancer with positive malignant cells (two of them presented with malignant ascites and one with cervical lymphadenopathy). One case (12.5%) for each of Neuroblastoma and Ewing sarcoma.

Concerning the relation of the pathological cause with the age of the participants, inflammatory causes were more common in the age group 10-15 years while congenital causes were more prevalent in the age group 1-5 years. The benign neoblastic lesions were more common in the age group 15-18, whereas the malignant neoplasms peaked between 5-10 years.

Regarding the gender distribution of pediatric lesions, inflammatory causes have equal sex distribution whereas the congenital causes are more prevalent in males. Benign lesions affected females mainly, while malignant neoplasms were more common in males **Table 3.**

Table 3: Relation of etiology of pediatric lesions to age, sex, and the site of the lesion.

Pathological Lesion	**Non-Neoplastic**				**Neoplastic**		**P-Value**
Pathological cause	**Inflammatory** No. (%)	**Congenital** No. (%)	**Others** No. (%)	**Normal biopsy** No. (%)	**Benign** No. (%)	**Malignant** No. (%)	
Age							
< 1 year	4	0	1	0	0	0	< 0.001
1-5 yrs	15	1	1	0	0	1	
5-10 yrs	16	0	0	2	2	4	
10-15 yr	25	1	11	0	9	1	
15 and < 18 yrs	20	0	5	0	17	2	
Gender							
Males	40	2	8	0	0	5	< 0.001
Females	40	1	10	2	28	3	
Site of the lesion							**Total**
Lymph node	65	0	0	0	0	4	69
Breast	1	0	2	2	23	0	28
Bone and soft tissues	7	2	6	0	2	0	17
Thyroid	1	0	9	0	0	0	10
Fluid cytology	4	0	0	0	0	2	6
Skin	1	0	0	0	3	0	4
Kidney & Adrenals	0	0	0	0	0	2	2
GIT	1	0	1	0	0	0	2
Total	80	2	18	2	28	8	**138**
	102				**36**		

Discussion:

Fine needle aspiration cytology is a very valuable diagnostic tool in the pediatric population but one of its disadvantages is that it is difficult to repeat it in children if this is necessary.

In the present study, there was a female predominance, female to male ratio is 3:2 which is against the finding of Maheshwari et al who reported a male predominance male: female ratio being 2: 1 [17]. The commonest age group in the current study was 10-15 years accounting for 47 (34.1%). In a study done by Prathima et al [18] the most common age group of the participants was 11-18 years (180, 55%) which is more or less consistent with our finding that the age group 11-18 was the most prevalent accounting for (66%).

The most common primary site from which the biopsy was taken was lymph node 69 (50%) which is similar to the findings of Koteswari et al and Agarwal et al [19, 20], followed by the breast, subcutaneous tissues then the thyroid. Whereas the most common pathological cause was inflammatory followed by benign neoplastic lesions, malignant neoplasm, and then congenital causes. This finding was in concordance with the findings of Wadone et al and Mohan et al [5, 21] as for inflammatory and benign neoplastic lesions.

In the current study in the majority of lymph node aspirates 42(60.9%) the cytology revealed reactive lymph node hyperplasia this typically supports what was described by Annam et al who reported the same findings [22]. It is also similar to Ahmed et al study which reported reactive lymphadenopathy as the most common cytopathological cause (64%) followed by granulomatous lymphadenitis (26%) and malignancy in (10%) [23]. The most involved lymph node group was cervical followed by submandibular this is similar to what Ronchi et al have found [24]. Other lymph node groups include axillary, generalized lymphadenopathy, periauricular, and supraclavicular.

Regarding the FNAC taken from the breast, the most common cytopathological cause was fibroadenoma of the breast 20 (71.4%), this is lower than wahat Rao et al had found who reported 93.8% of the specimens showed fibroadenoma [25] and a bit higher than what Rajini and Amita reported (62.2%) [26]. Other cytopathological patterns of the breast FNAC were fibrocystic changes of the breast 3(10.7%), 1 (3,6%) breast abscess, gynecomastia (two male cases), and in two instances the cytology showed normal unremarkable breast tissue.

The current study showed that the commonest cytopathological pattern of the thyroid FNAC was colloid goiter (50%) this is consistent with the findings of a study done in India [27].

The most encountered malignant tumors were Hodgkin lymphoma and metastatic cancer 3(37.5%) for each, followed by neuroblastoma and Ewing sarcoma 1(12.5%) for each. This differs from the result of Bhagat and Jandial [28] who reported Hodgkin and non-Hodgkin lymphoma and Ewing's sarcoma to be the most common malignant lesions.

In the present study fluid cytology for pleural effusion showed an inflammatory pleural effusion in all cases. Whereas in those of ascites, the cause was found to be metastatic cancer (Positive malignant cells). This is against what was found by Savitri Singh et al who reported the cytology of pleural aspirates 60% due to tuberculous, 30% empyema, and 10% lymphoma(T-NHL) while the two samples of ascitic fluid were due to tuberculosis [29].

The current study found that the inflammatory causes affected both sexes equally whereas the congenital causes are more prevalent in males. Benign lesions almost always affected females only this gender difference is statistically significant (P-value < 0.001) which is most likely explained by the surge in the incidence of fibroadenoma in adolescent girls, while malignant neoplasms were more common in males.

We found that the most common soft tissue lesions were eumycetoma followed by lipoma and cysts (Hemorrhagic or Infected), this a bit differs from the findings of Sanjay and Sarvesh who reported lipoma, giant cell tumor of the tendon sheath, and chondroblastoma as the most common soft tissue lesions [30].

Conclusion:

Fine needle aspiration is a safe and reliable method that helps diagnose many pediatric lesions. The current study showed that the majority of the participants were females, and the common age group was 10 - 15 years representing 47(34.1%) the steady surge in the incidence of benign breast conditions during adolescence can explain this finding. The most common biopsy site was lymph nodes (50%) followed by breast (20.3%), and the most commonly involved lymph node group was the cervical (81%) lymph nodes, which is consistent with the existing literature. Fortunately, non-neoplastic lesions were the most common underlying cytology (73.9%) of which the most common underlying cytology was inflammatory lesion (78.4%). The neoplastic lesions constituted 26.1% of the total specimens of which 28(20.3%) showed benign neoplastic growth whereas malignant neoplasia was encountered in 8(5.8%) specimens.

Authors´ contribution to the research

1. **Elfatih Mirghani Mohammed Salih**: Preparation and designing of the proposal, data entry and analysis, writing and revision of the manuscript.
2. **Moataz M Alhasan:** Preparation of the research proposal, writing and revision of the manuscript.
3. **Elsadig Ahmed Adam Mohammed:** Preparation of the research proposal, data collection, and revision of the manuscript.
4. **Rabei Mansour Elbadry:** Preparation of the research proposal, writing and revision of the manuscript.
5. **Mohammed Eltoum Hamed Azoz:** Preparation of the research proposal, Data collection, and revision of the manuscript.
6. **Elsharif Ahmed Bazie:** Preparation of the research proposal and revision of the manuscript.
7. **Khalid Al Awad A. Mohammed:** Preparation of the research proposal and revision of the manuscript.

All authors read and approved the final manuscript.

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

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