

# Pattern of pediatric fine needle aspiration cytology and its utility in management of head and neck swellings in a tertiary hospital in northwestern Nigeria

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## Abstract

Childhood malignancies have emerged as an important cause of morbidity and mortality globally. Diagnosis need to be accurate and fast to reduce this. Fine Needle Aspiration Cytology (FNAC) is an accepted modality employed in the diagnosis of adult and pediatric tumors. This study aims to review the pattern of pediatric FNAC from all sites done over a 10-year period, and its utility in the management of head and neck swellings. Records of all pediatric FNAC within the 10-year study period were retrospectively retrieved and analyzed. Data regarding age, sex, site of biopsy and FNAC diagnoses were extracted. Subsequent histologic diagnoses from the head and neck region were correlated with initial FNAC diagnoses from the same region. Data were presented in frequencies and percentages in tabular form. Accuracy, sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of head and neck lesions were calculated. A total of 301 pediatric FNAC were recorded. There were 160 (53.8%) males

and 141 (46.2%) females with a M: F ratio of 1.1:1. The average age was  $7.2 \pm 3.9$  years. The highest frequency of 134 (44.5%) was seen in the 5-10 years age group. Benign cytological diagnoses were rendered in 243 (80.7%) while the remaining 58 (19.3%) were malignant. Of the total, 244 FNAC were from head and neck Swellings, 209(80.7%) were benign while the remaining were malignant. Sixty-two (62) cases of head and neck FNAC had subsequent histologic tissue diagnoses (considered the gold standard) which were compared with prior FNAC results. FNAC of the head and neck showed an accuracy 82.1%, sensitivity of 53.0%, specificity of 93.3%, PPV and NPV of 75.0% and 84.0% respectively. FNAC is an easy, fast, cheap and minimally invasive screening tool that is accurate for diagnosis in the management of pediatric head and neck swellings in our setting.

## Introduction

Childhood cancer mortality is declining in developed nations especially in European and North American populations.<sup>1</sup> In developing countries of Africa and Asia however, childhood malignancy is still an important cause of morbidity and mortality together with other known causes like infectious diseases and malnutrition.<sup>2,3</sup> Most of these malignancies are embryonal with varying reports as to the commonest types. In developed countries like the USA, Central Nervous System (CNS) tumors are the commonest tumors in children, followed by neuroblastomas and Non Hodgkin lymphomas.<sup>4</sup> The picture is quite different in Africa and parts of Asia where Non Hodgkin lymphoma especially Burkitt lymphoma are the commonest, followed closely by Nephroblastoma and Retinoblastoma.<sup>5-9</sup>

Fine Needle Aspiration Cytology (FNAC) is a modality of diagnosis that is employed in the early diagnosis of tumors such as Nephroblastoma, Neuroblastoma, head and neck tumors.<sup>10-12</sup> It has the advantages of a quick turn-around time, low cost, minimal risks of complications and of being less invasive compared to open or excisional biopsy. Despite the apparent advantages of FNAC, there are concerns about the risk of tumor seeding in the needle track during aspirations in certain disease entities such as ovarian cancer.<sup>13</sup> Its high sensitivity and importance as a veritable diagnostic tool has also been documented in various studies conducted in India,<sup>12</sup> Iran<sup>14</sup> and Nigeria.<sup>15,16</sup> Various studies have compared results from FNAC and histology and found sensitivity and specificity ranging between 50% to 100%.<sup>17-21</sup> Although the incidence of FNAC use has increased, some studies raise questions regarding its accuracy and utility, especially in the diagnosis of lymphomas.<sup>22</sup> In the management of pediatric head and neck Swellings, several studies that compared FNAC preliminary diagnosis with the final definitive histological diagnoses have shown

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the usefulness of FNAC in terms of its high sensitivity and specificity and in avoidance of unnecessary surgical biopsies for benign lesions.<sup>16,17,22-24</sup>

This study aims to review the pattern of all pediatric FNAC cases in our hospital over a 10-year period (2006-2015) and to assess the utility of FNAC in terms of its accuracy in the management of head and neck swellings in our setting.

## Materials and Methods

This was a retrospective review of all FNAC done on children between the ages of 0-14 years over a 10-year study period from January 2006 to December 2015. Relevant data was collected from records of the Pathology department of the tertiary hospital. Information obtained from the records included age, sex, site of biopsy and the cytologic (FNAC) diagnoses.

All the archived FNAC slides used for the study were retrieved. All the fine needle aspirations (FNA) smears for the archived slides were carried-out using 23G needle and 20ml syringe using either free-hand or with a Cameco syringe holder. The aspirates were then smeared on frosted-end of the slides which were fixed in alcohol or air dried and then stained with Papanicolaou (PAP) and Diff-quick stains respectively. Only FNACs with results (either benign, specified type, malignant or unspecified) were included in the study. Smears reported as inadequate for diagnosis were excluded. Data generated was entered into a spread sheet and analyzed using Statistical Package for Social Sciences (SPSS) version 16. Quantitative variables were summarized using mean and standard deviation while the Qualitative variables were expressed as frequencies and percentages.

Subsequent available definitive histologic diagnoses (considered the gold standard) of follow-up cases of the FNACs involving the head and neck region were also retrieved from the records. The

initial cytologic (FNAC) diagnoses of aspirates from the head and neck region were then correlated with their final histologic tissue biopsy diagnoses. The accuracy of the pediatric FNAC of the head and neck region was determined by calculating the sensitivity, specificity, PPV and NPV.

## Results

Over the 10-year study period (2006-2015), 301 pediatric FNAC from all sites were recorded. There were 160 (53.8%) males and 141 (46.2%) females with M: F ratio of 1.1:1. The average age was 7.2±3.9 years. The age ranged between 1 month and 14 years. The highest frequency of 134 (44.5%) was in the 5-10 year age group. The 0-5 year age group had 88 (29.2%) cases while the >10-year age group had 79 (26.2%), Table 1.

Benign cytological diagnoses were rendered in 243 (80.7%) cases while the remaining 58 (19.3%) were malignant. The benign cases included reactive non-specific adenitis (82 cases, 27.2%), granulomatous inflammation (36 cases, 12.0%) tuberculosis (32 cases, 10.6%), suppurative inflammation (24 cases, 8.0%) and others [reported as just "benign" but not specified] Table 1.

There were 58 (19.3%) cases of malignancy reported, 39 of which were reported as malignant without type specification and required further definitive histologic assessment. Among the specified cytological diagnoses, Burkitt lymphoma predominated with 8 (2.7%) cases followed by Hodgkin lymphoma with 6 (2.0%) cases. Other cytological diagnoses and their frequencies are as depicted in Table 1.

Sites of FNA included the head and neck (244 cases, 81.1%), intra-abdominal mass (15 cases, 5.0%), cerebro-spinal fluid (CSF) (7 cases, 2.3%), ascitic fluid (3 cases, 1.0%) and other sites (32 cases, 10.6%) which included the breast, limbs, chest wall etc. (Table 2).

Out of the 244 cases of head and neck FNAs done, 209

**Table 1. Sex and age distribution of Paediatric cytologic diagnoses.**

Cytodiagnosis	Sex		Age group (years)			Total
	Male	Female	0-<5	5-10	>10	
<b>Benign</b>						
Reactive adenitis	39	43	31	32	19	82 (27.2)
Granulomatous inflammation	20	16	12	10	14	36 (12.0)
Tuberculosis	18	14	13	11	08	32 (10.6)
Suppurative inflammation	15	09	10	12	02	24 (8.0)
Others (unspecified)	32	37	15	29	25	69 (23.0)
Subtotal	124	119	78	99	66	243
<b>Malignant</b>						
Hodgkins lymphoma	04	02	-	03	03	06 (2.0)
Non-Hodgkins lymphoma	02	-	-	01	01	02 (0.7)
Burkitts lymphoma	05	03	-	06	02	08 (2.7)
Nephroblastoma	01	-	01	-	-	01 (0.3)
Metastatic carcinoma	01	01	-	01	01	02 (0.7)
Malignant (unspecified)	23	16	09	24	06	39 (13.0)
Subtotal	36	22	10	35	13	58
Total (%)	160 (58.2)	141 (46.8)	88 (29.2)	134 (44.5)	79 (26.2)	301(100.0)

(80.7%) were reported as benign and 35 (19.3%) as malignant (Table 2). Among the head and neck FNA, the most common site of aspirates was the lymph node with 233 (95.5%) cases. This was followed by jaw mass (5 cases, 0.2%), salivary gland (5 cases, 0.2%) and scalp (1 case, 0.1%) as shown in Table 3.

Only 62 (25.4%) of the reported FNACs of the head and neck site follow-up had subsequent histologic tissue biopsy for confirmation of diagnoses. These 62 cases were correlated with the preliminary cytologic (FNAC) diagnoses. Benign cytologic (FNAC) diagnoses were confirmed as benign by tissue histology (True negatives) in 42 (67.7%) out of the 62 cases while 9 (14.5%) cases reported as malignant on FNA were confirmed as malignant by histology (True positives). Diagnostic errors were encountered in 8(13.0%) (False negatives) cytological benign cases and 3 (4.8%) (False positives) cytological malignant cases which were later confirmed as malignant and benign respectively on histologic evaluation (Table 4).

Among the 8 false positives, four (4) cases of Hodgkin lymphoma were reported as reactive non-specific adenitis. Other false positive and false negative diagnoses are shown in Table 5.

The validity of FNAC of head and neck region as confirmed by definitive histologic tissue biopsy was found to have an overall accuracy of 82.1%, sensitivity of 53.0%, specificity of 93.3%, PPV and NPV of 75.0% and 84.0% respectively.

## Discussion

This study has shown overall high accuracy of FNAC of pediatric head and neck swelling. We recorded overall accuracy of 82.1%, a modest sensitivity of 53.0%, and high specificity, positive (PPV) and negative predictive values (NPV) of 93.3%, 75.0% and 84.0 % respectively. The study which included all FNAC cases from all sites over the review period, showed a slight male patient predominance and an average age of presentation of 7.2 years. The head and neck were the commonest site of biopsy.

A similar study conducted by Khdhayer *et al.*<sup>17</sup> in Iraq, found a comparable sensitivity, specificity and accuracy of 50%, 90% and 70% respectively. However, in keeping with documented high accuracy of FNAC in diagnoses of pediatric head and neck swelling, Rapkiewicz *et al.*<sup>23</sup> in the US recorded a sensitivity of 93% and specificity of 100%. Also, similar studies by Prathima in India<sup>21</sup> and AlQudehy in Saudi Arabia<sup>26</sup> revealed high specificity and predictive values respectively.

The modest sensitivity of FNAC recorded by this study as compared with above mentioned studies may be due to increased number of false negatives. As shown in Table 5, a total of eight

false negative diagnoses and three false positive diagnoses were made. Four cases of reactive adenitis were histologically confirmed as Hodgkin lymphoma and two of the three false positives were also reported as reactive adenitis. Hodgkin lymphoma may be misdiagnosed as reactive adenitis on cytology when Reid-Stenberg (R-S) cell or its variant is relatively sparse or absent or may be masked by preponderance of background reactive lymphoid cells.<sup>22</sup>

Some studies report limitations of FNAC in accurately diagnosing lymphoma and sensitivity of FNAC for the diagnosis of lymphoma reported in various studies ranges between 62 to 100%. Although pathologists feel that FNA has limited efficacy in the

**Table 2. Site distribution of fine needle biopsies.**

Site of biopsy	Diagnosis		Total (%)
	Benign (%)	Malignant (%)	
Head & Neck	209	35	244 (81.1)
Intra-abdominal mass	2	13	15 (5.0)
CSF	5	2	7 (2.3)
Ascites	3	0	3 (1.0)
Other sites	24	8	32 (10.6)
Total (%)	243(80.7)	58(19.3)	301 (100.0)

**Table 3. Distribution of site of FNAC of head and neck swellings.**

Site of FNA	Diagnosis		Total (%)
	Benign (%)	Malignant (%)	
Lymph nodes	204	29	233 (95.5)
Jaw mass	1	4	5 (0.2)
Salivary gland	3	2	5 (0.2)
Scalp	1	0	1 (0.1)
Total (%)	209 (80.7)	35 (19.3)	244 (100.0)

**Table 4. Histologic confirmation of cytologic diagnoses of head and neck region.**

	Cytology (FNAC)		Total (%)
	Benign (%)	Malignant (%)	
Benign (%)	42(67.7)	3 (4.8)	45 (72.6)
Malignant (%)	8 (13.0)	9 (14.5)	17 (27.4)
Total (%)	50 (80.6)	12 (19.4)	62 (100.0)

**Table 5. Shows the false positive and negative cases.**

Type of error	Site	FNAC diagnosis	Histologic diagnosis
False positive	Lymph Node	Reactive adenitis	Hodgkin lymphoma
	Lymph Node	Reactive adenitis	Hodgkin lymphoma
	Salivary gland	Benign	Muco-epidermoid carcinoma
	Lymph Node	Benign	Non-Hodgkin lymphoma
	Pre-auricular	Benign	Embryonal rhabdomyosarcoma
	Forehead	Benign	Solitary fibrous tumor
	Lymph Node	Reactive adenitis	Hodgkin lymphoma
	Lymph Node	Reactive adenitis	Hodgkin lymphoma
False negative	Lymph Node	Malignant	Reactive adenitis
	Salivary gland	Hodgkin lymphoma	Pleomorphic adenoma
	Lymph Node	Hodgkin lymphoma	Reactive adenitis

evaluation of lymph nodes and lymphoma, its use is increasing.<sup>20,22</sup> Ancillary diagnostic techniques used in modern pathology practice such as immunohistochemistry and flow cytometry can be applied to standard cytology practice to improve the accuracy of lymphoma diagnosis.<sup>22</sup> In our study, 95.5% of the aspirates of head and neck swellings were from lymph node and despite the false negative cases, we feel that with the high specificity and predictive value, lymph node FNAC still has a major role in screening for lymphoma and avoiding unnecessary surgical biopsy for reactive adenopathy.

Malignant epithelial tumors of the salivary glands in pediatric patients are rare with an annual incidence of 0.8 cases per 1 million children and adolescents.<sup>27</sup> There were a total of five (0.2%) cases of salivary gland FNACs out of which three benign cases were correctly diagnosed. A case of Muco-epidermoid carcinoma was initially reported as benign while a case of pleomorphic adenoma was misdiagnosed as lymphoma (Table 5). Literature review has shown a wide variation in the sensitivity and specificity of FNAC for salivary gland swelling in different populations.<sup>18</sup> The number of salivary gland lesions in our study is quite low to enable us make any reasonable conclusions.

Optimal results from FNAC is dependent on the skill and experience of the cytopathologist, and also on effective communication between the clinician and the pathologist.<sup>23,26</sup> As a training institution, some of the aspiration procedures were carried out by trainees with varying levels of competence and this will undoubtedly affect the adequacy of diagnostic material obtained. This will also affect the overall accuracy of the FNAC and may partly explain the modest sensitivity obtained by the study.

Of the 301 cases from all sites that underwent FNAC during the study period, 243 (80.7%) were reported as benign. Majority of these benign cases were spared from unnecessary and expensive surgical biopsies. Reactive non-specific adenitis, granulomatous inflammation and tuberculosis constituted 34.0% (82/243), 14.8% (36/243) and 13.2% (34/243) of the benign cases respectively. Most of the studies on FNAC involving lymph node swellings found reactive non-specific adenitis to be the most common benign outcome.<sup>16,17,21,23,28</sup> This study also revealed reactive adenitis as the most common benign diagnosis in FNAC of lymph nodes. Similar pattern was also reported by Silas *et al.*<sup>16</sup> in Nigeria, Prathima<sup>21</sup> and Singh<sup>28</sup> both in India, and Rapkiewicz<sup>23</sup> in the US who documented 71.2%, 65.2%, 71.0% and 66.0% respectively. In agreement with reports of high incidence of TB in developing countries, this and the aforementioned studies showed identical proportions of TB among benign cytologic lymph node biopsies. All the 32 (10.6%) cases of TB in this study were confirmed using Ziehl Nelson (ZN) stains enabling prompt institution of treatment. Other authors of identical studies from developing countries such as ours reported comparable proportions for TB adenitis ranging from 9.3-17.1%.<sup>16,21,28</sup> There were 36 (12.0%) cases reported as granulomatous inflammation documented by this study. Most of these cases were negative for acid fast bacilli stain (AFB). This does not however exclude tuberculosis. Fungal infection is another cause of granulomatous inflammation in our practice.

Finally, this study has shown the utility of FNAC and recorded a high specificity and NPV which confers a high level of confidence in the exclusion of malignancy in clinically suspicious swellings of the head and neck among pediatric age group. Majority of the cytological benign diagnoses such as TB sufficed for the further management of these patients and thus avoided the need for surgical biopsy.

## Conclusions

FNAC is a cheap, fast, relatively non-invasive, and reasonably accurate tool for diagnoses of pediatric head and neck swellings in our hospital. Though with modest sensitivity, it has high negative predictive value, high specificity, and thus plays an important role in preventing unnecessary, expensive and invasive surgical biopsy for benign swellings. It also allows for prompt non-surgical diagnosis of malignant lesions which will be followed-up by tissue biopsy. We recommend its improvement and continued utilization in the management of head and neck swellings in our center.

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