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ORIGINAL RESEARCH

A 17-year study of paediatric cytopathology in a tertiary hospital in Sokoto, Nigeria

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Abstract

Background: Cytopathology offers a rapid diagnosis of suspicious lesions, aiding prompt clinical judgment. The extent of the cytopathologic practice is variable, thus justifying the need to assess the frequency of its use in health care centres in resource-challenged settings.
Objectives: To assess the frequency of use of cytopathology services, the demographic features of the patients and the various diagnostic outcomes.
Methods: The study was a retrospective analysis of 17 years' records; including parameters like the basic demographics and cytomorphologic diagnoses in paediatric practice. Data was sought from histopathology department registers and cytopathologic request forms for patients in the age range of 0-15 years.
Results: The total number of the paediatric cytologic specimen was 930 constituting 12.3% of all cytologic specimens received in the study period. The mean age was 8.0 years with a range of 1 day to 15 years. There were 537/930 (57.7%) males and 378/930 (40.6%) females with a male-to-female ratio of 1.4:1. The specimens were obtained by fine-needle aspiration cytology in 596/930 (64.1%) cases or smears of exfoliative specimens in 334/930 (35.9%) cases. Most of the samples were obtained from children in 6 - 10 years age group. The commonest clinical indication for the cytology was "suspected malignancy" comprising 370/930 (39.8%) cases. The most frequent cytopathological diagnosis was "positive for malignancy", accounting for 232/930 (24.9%) cases.
Conclusion: Cytopathology practice in a resource-poor setting remains a useful tool in the preliminary evaluation of lesions.

Keywords: Childhood malignancies, Cytology, Fine needle aspiration, Paediatrics, Smears, Sokoto.

Introduction

Cytopathology is an arm of pathology that uses cytology either as a primary or ancillary tool, to arrive at diagnosis (or prognosis) of a wide spectrum of diseases. Cytology is the microscopic examination of appropriately stained individual cells obtained from the body through exfoliation, imprints or aspiration. The practice has evolved. Its humble beginnings date as far back as 1868.

Since then, it has become a major discipline offering rapid and cost-effective (and sometimes sole) means of diagnosis. [1-4] It is currently practiced as either exfoliative cytology or (fine needle) aspiration cytology. The former includes gynaecology (such as Pap smear), bronchial washing, sputum, urine, pleural, pericardial and peritoneal fluid while the latter comprises aspiration of palpable and non- palpable lesions.

The justification for this study lies in the fact that the availability and accessibility of healthcare in resource-poor regions of the world (including sub-Saharan Africa) remains a major challenge. These challenges include lack of resources, low budgetary allocations to health care by governments, scarcity of well-trained personnel and paucity of laboratory diagnostic capacities. These ultimately result in late presentation with an advanced disease by patients. These observations underscore the need for rapid cost-effective diagnostic techniques. Cytopathology is poised to serve such a purpose when the indication arises. [5]

Atanda *et al.* have observed that the mortality rate in paediatric malignant neoplasms remains high in resource-poor regions and attributed these to a worsened global economic downturn. In the same vein, Tanko *et al.* observed that several Africa sub-region, including Nigeria, are reporting an increase in childhood malignant neoplasms and this underscores the need to develop among other things, diagnostic tools that are accessible and affordable. [6, 7]

Malami *et al.* have noted that little attention is given to childhood neoplasia in the resource-challenged regions of the world. In another report, Malami observed the low use of fine-needle aspiration cytology in Nigeria. [8, 9] Therefore, policymakers must have data at their disposal to guide decision making in funding cost-effective diagnostic procedures if the tide must be stemmed. Also, because of the neglect, there are relatively fewer paediatric cytopathology publications in contrast with adult care where it is an established practice as attested to by a large number of publications. [10]

Cytopathology offers a rapid diagnosis of suspicious lesions and aids prompt clinical judgment. It can also be used to screen for disease (for example pap smears of the cervix uteri to screen for premalignant lesions for cancer, anal smears for cancer of the anus and breast fine-needle aspiration cytology for cancer of the breast). [11-13] The practice of cytopathology is variable, depending on the sophistication of the centre and its geographic location. However, the practice applies to all ages and both sexes. [6, 14] Paediatric cytopathology, especially in health facilities situated in resource-poor regions of the world, remains an under-utilized practice. [6, 15] The specimen ranges from fluids (effusions, aspirates) to those obtained via fine-needle aspiration biopsy (FNAB). The latter specimen can be obtained via palpation or with an ultrasound scan guide. Several studies have demonstrated the advantages of the procedure and these include high sensitivity, specificity, cost-effectiveness, avoiding unnecessary surgical biopsy, safety, and reliability in confirming suspected malignancy. [16-19] Helson and Wong also noted that the procedure is simple to perform and useful in decision making. [20, 21] On the other hand, there are contraindications, harmful effects or complications such as bleeding or haematoma or pneumothorax. [22, 23]

While some studies in Nigeria [6, 24-27] have demonstrated the positive role of cytopathology in the management of lesions in adults, there is sparse information concerning the extent of use and relevance of cytopathology in paediatric practice, especially as it pertains to the practice in resource-poor settings.

This study is aimed at assessing paediatric cytopathology and the frequencies of various

diagnostic outcomes in Usmanu Danfodiyo University Teaching Hospital over seventeen (17) years. Specifically, it shall assess some basic demographic features of the paediatric age group who had a cytopathological examination, determine the clinical indications warranting request of cytological examination, ascertain the frequencies of various diagnoses and look at time trends in the use of cytopathological services in the centre. It is hoped that the findings of this study, being the first of its kind in this centre, shall bring forth the extent of use of cytopathology services and add to the relatively sparse body of literature on paediatric cytopathology. It can also underscore the need for channeling resources towards training specialists and providing them with enabling tools for optimal practice. Also, it can encourage clinicians to make more frequent requests for the services.

Methods

The study was conducted in the Department of Histopathology of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, a tertiary health institution situated in the north-west, Nigeria. This hospital provides tertiary health care services to Sokoto, Kebbi, Zamfara and Niger States. It also receives referrals from the Niger Republic, a neighbouring country. Services rendered in the histopathology department of the hospital include histopathology of surgical biopsies and research specimens, cytopathology (including fine needle aspiration cytology), frozen sections, immunohistochemistry, and autopsy. Ethical clearance was obtained from the Ethics and Research Committee of the institution (UDUTH/HREC/2018/No. 721).

The patients had earlier been evaluated at the paediatric clinics or wards in the hospital. The attending paediatrician had filled out the histopathology requisition form and referred them to the Department of Histopathology for fine-needle aspiration of suspected lesions by the histopathologists. In some other cases, fluids aspirated by the paediatricians in the course of clinical management were also sent to the histopathology laboratory for processing. The processing essentially involved making smears on glass slides, fixation in alcohol and staining with Papanicolaou stain or hematoxylin and eosin stains. The slides were then reported by histopathologists using a light microscope. However, cell blocks and special stains (such as Gomori's stain for fungi) were not done. Correlation with a surgical biopsy specimen was not done in most instances. The results of the microscopic evaluation of the stained smears are usually classified as: "unsatisfactory/inadequate", "benign/negative for malignancy", "suspicious" and "malignant".

In the present study, the sampling method involved accessing the histopathology department records, (reception registers, bench books, and request forms) for all the cases registered as cytology specimen over the period between 1st January 2001 and 31st December 2017 (17 years). These were consecutively selected and the data extracted specifically included: age, sex, site of biopsy, clinical indication and cytological diagnosis. Cases with missing or incomplete information were excluded from the study. The data generated were entered into the 2007 Edition of the Microsoft® Excel statistical package spread-sheet. The data were validated and exported to Statistical Package for Social Sciences software for analysis. The results were presented as frequency distribution tables for demographic features, body sites from which specimens were obtained, clinical indications warranting the cytology test and cytological diagnosis.

Results

Nine hundred and thirty (930) paediatric cytology specimens were studied; these constituted 12.3%

of all cytology specimens received in the 17 years' study period. The mean age was 8.0 years with a range of 1 day to 15 years. There were 537/930 (57.7%) males and 378/930 (40.6%) females with a male-to-female ratio of 1.4:1 (See Table I). The specimens were obtained by fine-needle aspiration cytology in 596 (64.1%) cases and smears of exfoliated cells 334 (35.9%) (See Table I).

Table I: Clinico-demographic distribution of patients who required a Cytology Specimen.

Characteristics		Frequency (n = 930)	Percentage
Age groups (years)			
	<1	77	8.3
	1-5	256	27.5
	6-10	339	36.5
	>15	258	27.7
Sex			
	Male	537	57.7
	Female	358	40.6
	Unspecified	15	1.6
Nature of specimen			
	FNAB	596	64.1
	Smear	334	35.9

Most of the specimens were obtained from the 6–10 years age group with 339/930 (36.5%). In this modal group, there were 205 (61.9%) males and 125 (38.1%) females. The clinical indications warranting the procedure varied with the commonest being "suspected malignancy" in 370/930 (39.8%) cases (See Table II).

The most frequent cytopathological diagnostic description was "positive for malignancy" in 232/930 (24.9%) cases; this was closely followed by "benign/negative for malignancy" in 227/930 (24.4%) cases. Forty-nine (5.3%) had changes suspicious of malignancy. Malignancies were frequently detected in the age group 6-10 years but least common in infancy. Among infants, all five malignant cases were males. Acellular and inadequate smears occurred in 6.1% and 3.4% cases respectively as shown in Table III.

One of the indications for cytology was sex determination as recorded in 65/930 (7%) cases with an attempt at visualizing "Barr bodies".

There has been a progressive increase in the annual frequency of use of the service in the hospital, with a peak in 2016 as shown in Figure 1. Figures 2 to 4 describe some of the abnormalities reported on cytological examinations.

Discussion

This study was a retrospective analysis of data accumulated over 17 years. Similar studies had previously reported an age range of 2 to 20 years. [17, 20, 28] The advantage of a study of two decades is that it gives a large sample size from which meaningful inferences can be drawn. Ours is a sample size of nine hundred and thirty (930) which is comparable to 889 in the study of Drut *et al* in Argentina. [17]

This sharply contrasts with others such as 136 (Marion *et al* from East Carolina, USA), 226 (Wong *et al.* from Ohio, USA), 389 (Cristina *et al.* from Indianapolis, USA), 2363 (by Helson *et al.* from New York, USA) and 7487 (Carol *et al.* from Indianapolis, USA).[17, 20, 28-30] Some of these frequencies were obtained over a relatively short period implying a heavier patient load and thus, underscoring the need for greater information dissemination in our locality to create awareness about the availability of the procedure. It should be noted that Malami *et al.* in Sokoto, Nigeria studied the usefulness of FNAB in the diagnosis

of Burkitt's lymphoma with a relatively small sample size of fewer than 30 patients over one year in the same centre. [15] Therefore, the present study comes in as a more exhaustive sampling with a much larger data pool and possibly, more sound inferences. Exfoliative cytology was also examined in the course of this study, considering all the possible diagnostic outcomes.

Table II: Clinical indications for cytological examinations

Clinical Indications	Frequency	Percentage
Breast Disease	31	3.3
Colloid Goitre	7	0.8
Genitourinary Disease	10	1.1
Inflammation/Infection	75	8.1
Lymphadenopathy	60	6.5
Malignancy	370	39.8
Metastatic Tumour	36	3.9
Salivary Gland Tumour	21	2.3
Sex Determination	65	7.0
Soft Tissue	93	10.0
Third Space Collection	50	5.4
Tuberculosis	112	12.0
Total	930	100.0

Table III: Cytolopathological Diagnoses

Cytologic diagnosis	Frequency	Percentage
Acellular	57	6.1
Barr Body Indeterminate	3	0.3
Barr Body Negative	34	3.7
Barr Body Positive	28	3.0
Inadequate	32	3.4
Inflammatory	219	23.5
Malignant	232	24.9
Negative/Benign	227	24.4
Reactive	49	5.3
Suspicious	49	5.3
Total	930	100.0

An extensive literature search revealed that there is a dearth of publications on paediatric cytopathology in resource-poor settings. The male-to-female ratio of 1.4:1 observed in the present study compares to 1.15:1 reported from the Kolar region of Southern India. [31] Atanda and Razack noted the usefulness of cytopathology in North-East Nigeria and India, with up to 100% and 77% detection rate for malignancies respectively. [6, 18] In the present study, the detection rate for malignancies was 87.1%, which is comparable to the former.

Razack's study (India) [18] reported that malignancies constituted 77% of their sample compared to 24.9% in the present study. In the Indian series, [18] 23% were benign cytological diagnosis similar to the 24% benign diagnosis observed in the present study. There a wide discrepancy is noted in the proportion of cases with the diagnosis of "positive for malignancy". This observation may not be unconnected to the fact that the Indian study focused on FNAB-obtained cytology specimens, unlike the present study which examined total cytology specimens (FNAB and exfoliative cytology). Also, the low

health-seeking behaviour of patients in the locality, high level of ignorance and poverty, which are all very pervasive in resource-poor regions, may have contributed to the present observation.

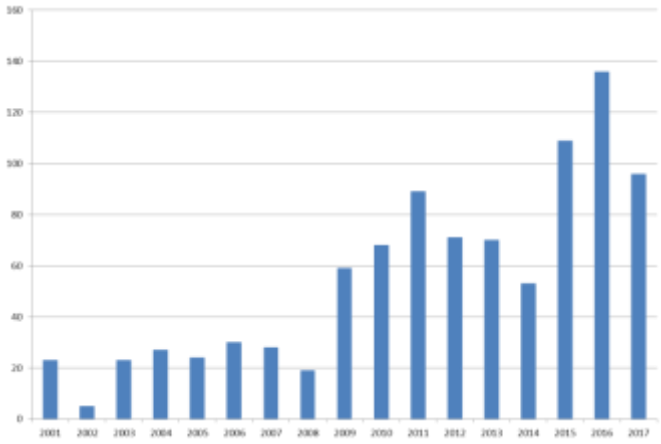

Figure 1: Annual distribution of the use of paediatric cytopathology services

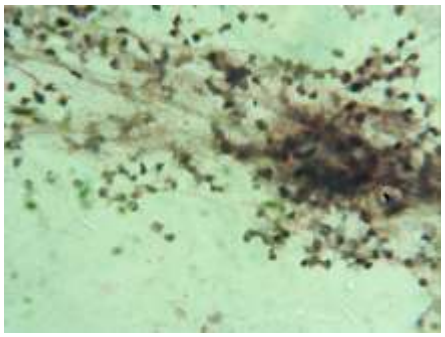

Figure 2: Photomicrograph of inflammatory cytology, showing viable and degenerating polymorphs in the background of fibrin deposits (Pap X 400)

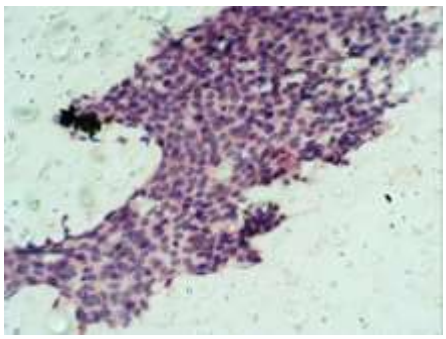

Figure 3: Photomicrograph of benign cytology, showing a tight cluster of bland epithelial cells (Pap X 400)

From other parts of the world, the reported rate of diagnosis of malignancy in cytology specimen includes 56.7% (Drut *et al.*), 45% (Wong *et al.*), 38% (Carol *et al.*) and 10.4% (Cristina *et al.*). [17, 21, 28, 30]

The higher percentages observed in the previous studies may reflect better health indices of these regions of the world including better health-seeking behavior. However, the lower figure in Cristina's study may be explained by the narrower age range captured in the study.

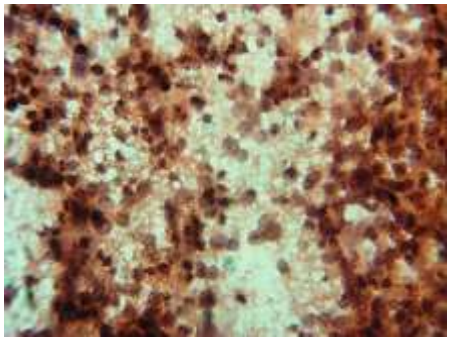

Figure 4: photomicrograph of malignant cytology, showing sheets of singles of hyperchromatic cells with coarse chromatin and small nucleoli (Pap X 400)

The diagnostic category referred to as "suspicious" represents a "grey area". [32] Expectedly, this ought to be infrequent as it places the clinicians in a dilemma on how to proceed with patient care. The rate of 5.3% observed in this study is higher than the figures reported from other centres. For example, Cristina *et al*. reported a rate of 2.5%. Another challenge is the "inadequate" category of cytopathological diagnosis which constituted 3.4% of the samples in the present study unlike 10.6% reported by Cristina *et al*. These observations highlight the need for closer collaboration between the pathologist and paediatrician and strict application of diagnostic criteria. [28]

The clinical implications of this study include the ability to make a diagnosis using cytology. This is apt for clinically suspected malignancies which constituted a total of about 44% of the clinical indications warranting cytologic examination in the present study. This reflects a high frequency of clinically suspected malignant neoplasms in this region of the world, similar to the observations of Sunttee *et al*., Atanda and Tanko *et al*. Atanda has brought to fore, the high rate of mortality from childhood malignancies and attributed this to several reasons including late presentation. The paediatric age group is amongst the vulnerable groups, so highlighted. Therefore, there is a need for a cost-effective and rapid means of achieving a diagnosis. Cytology easily comes to use in this scenario. The cost of cancer care is enormous and cytology can be done at minimum cost, yet with far-reaching diagnostic implications.

On a broader assessment, we observed a gradual increase in the use of cytopathological services in this center with a peak in 2016. We attribute this to increased awareness of its utility and availability of histopathologists at the centre (with attendant shortening of turn-around time). A drawback of this study was the inability to generate parameters like specificity, sensitivity and positive predictive values. These could not be done because of the lack of "gold standards" by way of corresponding histology sections for comparison. This happened because of very poor filling out of request forms, with no reference to whether tissue biopsy for histology was subsequently done. Furthermore, there is a high rate of loss of patients to follow up care, such that opportunities for subsequent tissue biopsies were lost. Some studies have shown positive predictive values ranging between 87% (Gregory) and 99.6% (Carol). [16, 30] In our resource-poor

scenario, many patients tended to present late with advanced-stage disease and high mortalities.

Conclusion

The practice of paediatric cytopathology even in resource-poor settings remains a useful tool in the preliminary evaluation of suspicious lesions. It can serve as a primary and ancillary diagnostic tool. As a recommendation, we advocate for capacity building by training and retraining of the pathologists and ancillary staff in this procedure and to improve the utilization of the services by encouraging clinicopathological interactive sessions between the paediatricians and the pathologists.

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