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ENHANCING SCREENING FOR CERVICAL CANCER PREVENTION: A COMPARATIVE STUDY OF LIQUID-BASED CYTOLOGY AND CONVENTIONAL PAP SMEAR AT AHMADU BELLO TEACHING HOSPITAL, NIGERIA.

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Abstract

Background

Cervical cancer is one of the cardinal public health problem of great concern, particularly in developing countries like Nigeria. Early detection of this disease through effective screening methods is crucial in reducing its' morbidity and mortality burdens. This study aimed to compare the effectiveness of liquid-based cytology (LBC) and conventional Pap smear in detecting cervical intraepithelial lesions among patients at Ahmadu Bello Teaching Hospital (ABUTH).

Methods

A total of 73 patients with abnormal cytology or histology results were analyzed. The mean age of participants was 47.5 years. Demographic information, including education status, was collected to assess the correlation between educational status and awareness of cervical cancer screening. Sensitivity and unsatisfactory result rates for LBC and conventional Pap smear were compared.

Results

The majority of participants (59.1%) had tertiary education, indicating a correlation between education level and awareness of cervical cancer screening. Over 50% of patients were unaware of Pap smear screenings, potentially contributing to delayed diagnoses. The sensitivity of LBC was found to be 100% for both squamous and glandular lesions, compared to 71.9% for conventional Pap smear. The rates of unsatisfactory results were lower in the LBC group (1.7%) compared to conventional Pap smear (4.3%).

High-grade squamous intraepithelial lesions (HSIL) were detected in 71.9% of LBC cases and 64.3% of conventional Pap smear cases.

Conclusion

Liquid-based cytology demonstrated superior sensitivity and accuracy in detecting cervical intraepithelial lesions compared to conventional Pap smear. Based on these findings, it is recommended that LBC be adopted as the primary screening method for cervical cancer. Additionally, there is a need for increased awareness and education regarding cervical cancer screening among the general population. Future prospective studies are essential to validate these findings and enhance cervical cancer prevention strategies.

Keywords: Cervical Cancer, Liquid-Based Cytology, Pap Smear, Screening, Public Health

Introduction

Cervical cancer is the most common malignancy among women in Northern Nigeria. While its incidence has steadily declined in developed countries, the opposite trend is observed in developing nations especially Sub-Sahara African. Approximately 500,000 women are diagnosed with cervical cancer annually, with 75% of these cases occurring in low- and middle-income countries. Cervical cancer poses a significant public health challenge for women in many regions of Sub-Saharan Africa and South Asia, where it is the second leading type of cancer and a leading cause of cancer-related death. The high burden of cervical cancer in these regions is attributed to a combination of high prevalence of human papillomavirus (HPV) infection and various sociocultural practices.

The risk factors for cervical cancer are multifactorial, including parity, early coitarche, age at menarche, multiple sexual partners, immunosuppression, and HPV infection. HPV is the most common sexually transmitted infection, with types 16 and 18 being the most closely associated with the progression to cervical cancer. HPV-16 is particularly carcinogenic, accounting for approximately 60% of cervical cancer cases, while HPV-18 contributes to about 10-15% of cases.

Epidemiological data indicate that organized screening programs significantly impact the morbidity and mortality associated with cervical cancer. The introduction of population-based screening using the Pap smear in the early 1960s aimed to detect and treat precancerous lesions, thereby preventing the progression to invasive cervical cancer. In advanced countries, the incidence of cervical cancer has considerably decreased due to the effective implementation of screening procedures in the latter half of the 20th century.

Cervical cytology screening is regarded as one of modern medicine's greatest success stories. Initiated by George Papanicolaou in 1943, this screening test has had a profound impact on reducing the incidence of invasive squamous carcinoma of the cervix and, consequently, cervical cancer mortality. Screening is defined as the systematic application of a test or inquiry to identify individuals at risk of a specific disorder, thereby facilitating early diagnosis and treatment for those who have not yet exhibited symptoms. Effective screening programs can significantly improve outcomes for select cancer types when appropriate tests are utilized, implemented correctly, and linked to comprehensive care pathways.

Recently, highly specific HPV DNA tests, such as the hybrid capture test and polymerase chain reaction (PCR) tests, have been developed for the detection of HPV in cervical and vaginal samples. These tests have shown great sensitivity and are likely to revolutionize the detection of HPV in the genital tract.

Cervical cytologic screening meets the World Health Organization (WHO) criteria for effective screening programs, including the disease's public health significance, availability of accepted treatments, diagnostic and treatment facilities, the presence of a suitable latent and symptomatic stage, acceptable tests for the population, understanding of the disease's natural history, agreed policies on treatment, and a cost-effective approach to health care. An optimal screening test should achieve these objectives with low costs while maintaining acceptable sensitivity and specificity.

However, the precise determination of sensitivity and specificity for cervical cytology is challenging, as the gold standard for comparison is histological evaluation of the entire cervical transformation zone. Ethical considerations prevent performing random cone biopsies solely to establish these rates. The limited

sensitivity of a single Pap smear necessitates repeated screenings in organized programs, and liquid-based cytology (LBC) has been suggested to improve sensitivity.

1.2 Problem Statement

According to the WHO, cancer is the second leading cause of death globally, responsible for 8.8 million deaths in 2015. Nearly one in six deaths worldwide is attributed to cancer, with approximately 70% of cancer deaths occurring in low- and middle-income countries. Cervical cancer ranks fourth in terms of both incidence and mortality.

In Northern Nigeria, the overall cost of illness for cervical cancer ranges from ₦191,338 ($524) for localized disease to ₦1,001,298 ($2,743) for metastatic disease. Direct medical costs account for up to 75.4% of these expenses, while indirect costs can reach up to 48% at various stages of the disease.

1.3 Justification

Liquid-based cytology has emerged as an alternative to conventional cervical cytology, yet controversy persists regarding its diagnostic accuracy. Cervical cancer remains the second most common malignancy among women worldwide, following breast cancer, and represents a significant national health issue. Many women who do not succumb to maternal mortality face the risk of dying from cervical cancer.

Given the high incidence of cervical cancer and the frequent occurrence of false-negative results in Pap smear screenings, there is a pressing need for studies that explore more effective diagnostic methods. Liquid-based cytology (LBC), including the liquid-based thin-layer method, has shown promise in reducing false-negative rates and improving sample quality. However, limited retrospective studies have been conducted to evaluate its effectiveness in comparison to conventional methods. This study aims to compare Thin Prep liquid-based cytology with conventional Pap smear, leveraging a laboratory with extensive experience in conventional Pap smear analysis.

Aim

To compare the effectiveness of liquid-based cytology versus conventional Pap smear in detecting cervical intraepithelial lesions and to assess factors influencing cervical cancer screening awareness at Ahmadu Bello Teaching Hospital.

Objectives

1. To evaluate the sensitivity and specificity of liquid-based cytology compared to conventional Pap smear in the detection of cervical intraepithelial lesions among patients.
2. To assess socio-demographic factors associated with awareness and utilization of cervical cancer screening among patients.
3. To analyze the prevalence of dysplastic lesions identified in the pathology records during the study period.
4. To recommend improvements in cervical cancer screening practices based on the findings of the study.

Methodology/Study Design

This study is a retrospective, comparative cohort design conducted at Ahmadu Bello Teaching Hospital (ABUTH), analyzing patient folders and records from the Pathology Department and Reproductive Health Clinic from January 2013 to December 2017. A composite proforma was developed to capture key components related to the study's objectives and included socio-demographic characteristics such as age, ethnic group, marital status, type of marriage, order of marriage, religion, occupation, educational status, economic status, previous Pap smear results, and number of sexual partners.

3.2 Study Population

The study population consists of records of patients with abnormal Pap smear results identified in the pathology laboratory whose colposcopy results confirmed dysplasia during the study period from January 2013 to December 2017.

3.3 Inclusion Criteria

1. All conventional Pap smear and liquid-based cytology results obtained between January 2013 and December 2017.

3.4 Exclusion Criteria

1. All Pap smear results classified as negative or inflammatory.
2. All inadequate or unsatisfactory smears.

3.5 Data Collection/Sampling Procedure

All eligible patient records within the study period will be reviewed and included in the analysis. The desired sample size will encompass all patients whose records meet the inclusion criteria.

Data Analysis

Data entry and analysis will be conducted using SPSS (version 22.0). Results will be presented in frequency distribution tables accompanied by percentages. Chi-square analysis will be employed to test the significance of categorical variables.

Results

This study involved the analysis of 73 patient folders referred for abnormal Pap smears during the study period. The mean age of the patients was 47.5 years. A significant relationship was identified between the age at menarche and the age at presentation. Patients who experienced early menarche (ages 8 to 12) tended to present before the age of 40, while those with menarche occurring between 13 and 17 years typically presented after the age of 45 (Table 2). Notably, over 50% of the patients reported an early age at menarche of less than 12 years (Figure 5).

Awareness of Pap smear screenings was notably low; more than 50% of patients were not aware of the test. The study also found a higher rate of unsatisfactory results with conventional Pap smears (1.8%) compared to liquid-based cytology (1%).

In terms of diagnostic performance, liquid-based cytology demonstrated a higher sensitivity in the detection of both squamous and glandular lesions, achieving 100% sensitivity against 71.9% for conventional Pap smear. Additionally, the positive predictive values were 96.5% for LBC and 69.7% for conventional Pap smear.

The study observed significant instances of false negatives associated with conventional Pap smear; however, the absence of true negative results in the records meant that specificity could not be calculated for either test. The detection of low-grade lesions was enhanced with liquid-based cytology, identifying 22.8% compared to 11.9% for conventional Pap smears, with histological analysis confirming that 43.5% of these samples were true low-grade squamous intraepithelial lesions (LSIL), a difference that was statistically significant for conventional Pap smear ($P = 0.007$).

Both screening methods successfully detected high-grade squamous intraepithelial lesions (HSIL), achieving detection rates of 64.3% with conventional Pap smear and 71.9% with liquid-based cytology, with no significant difference noted when compared to histological diagnoses. However, both tests demonstrated poor detection rates for glandular lesions.

Table 1: Socio demographic characteristics of study participants

Socio demographic characteristics	Frequency	Percentage
Ethnic group		
Hausa	53	57.6
Fulani	2	2.2
Yoruba	5	5.4
Igbo	6	6.5
Others	26	28.3
Marital status		
Single	3	3.5
Married	75	87.2
Divorced	1	1.2
Widow	7	8.1
Highest educational status attained		
None	9	13.6
Quranic	8	12.1
Primary	4	6.1
Secondary	6	9.1
Tertiary	39	59.1
Occupation of client		
House wife	42	45.2
Businessperson	26	28.0
Civil servant	25	26.9
Type of marriage		
Polygamy	35	41.7
Monogamy	49	58.3

Table 2: Age at menarche as risk profile for cervical cancer

Age at menarche (yrs)		Age of Client (years) =<29	30 – 34	35 – 39	40 - 44	45 – 49	50 – 54	55 – 59	=>60	Total	P-value
8-12	Count	0	0	6	3	3	0	1	3	16	0.000
	%	0.0%	0.0%	37.5%	18.8%	18.8%	0.0%	6.3%	18.8%	100.0%	
13-17	Count	1	7	8	11	23	16	3	0	69	
	%	1.4%	10.1%	11.6%	15.9%	33.3%	23.2%	4.3%	0.0%	100.0%	
18-22	Count	2	0	2	3	0	3	0	0	10	
	%	20.0%	0.0%	20.0%	30.0%	0.0%	30.0%	0.0%	0.0%	100.0%	
Total	Count	3	7	16	17	26	19	4	3	95	
	%	3.2%	7.4%	16.8%	17.9%	27.4%	20.0%	4.2%	3.2%	100.0%	

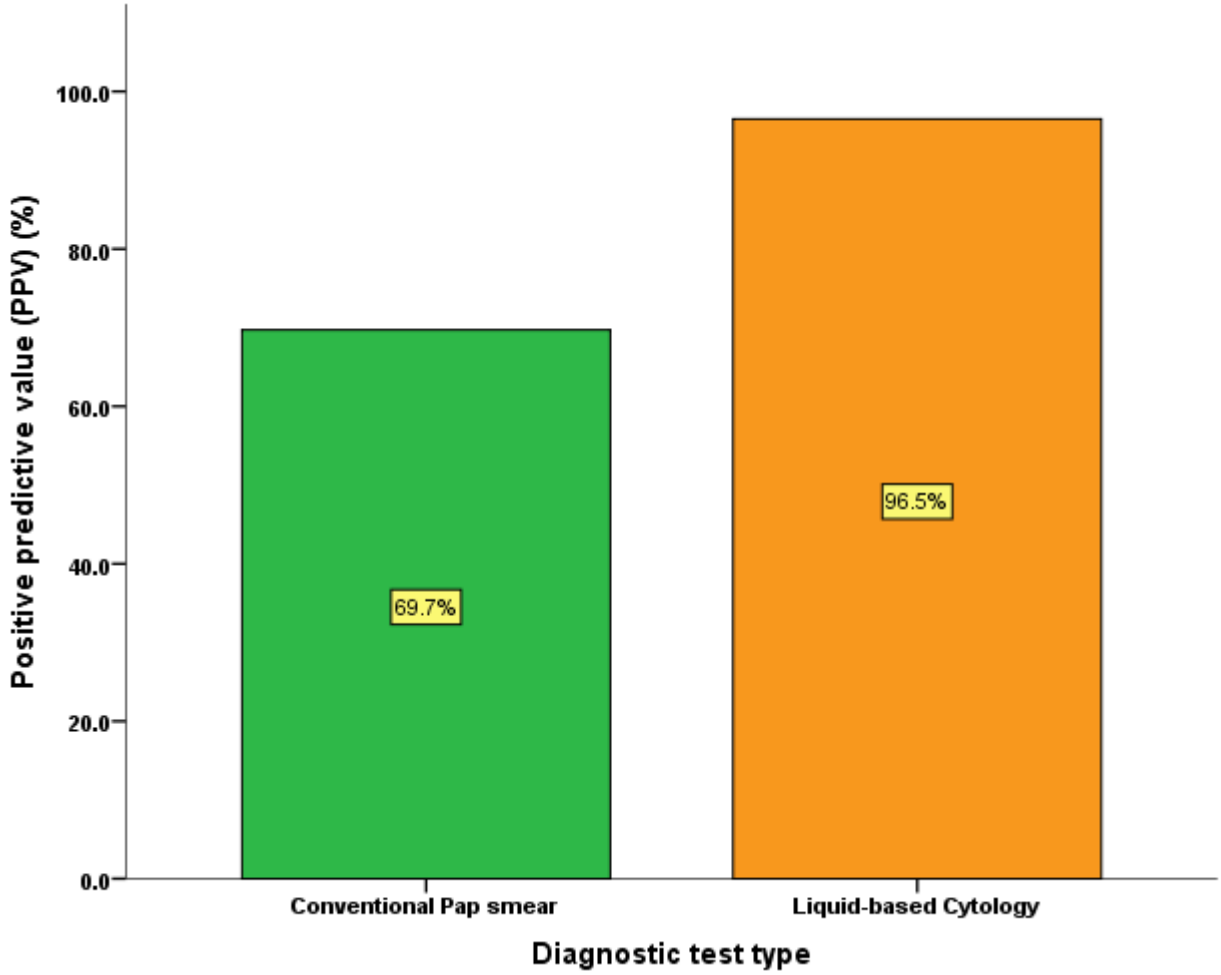

Figure 1: The positive predictive value as determinant of the effectiveness of the two diagnostic screening methods. The comparison between liquid-based cytology and conventional Pap smear screening methods in detecting cervical lesions.

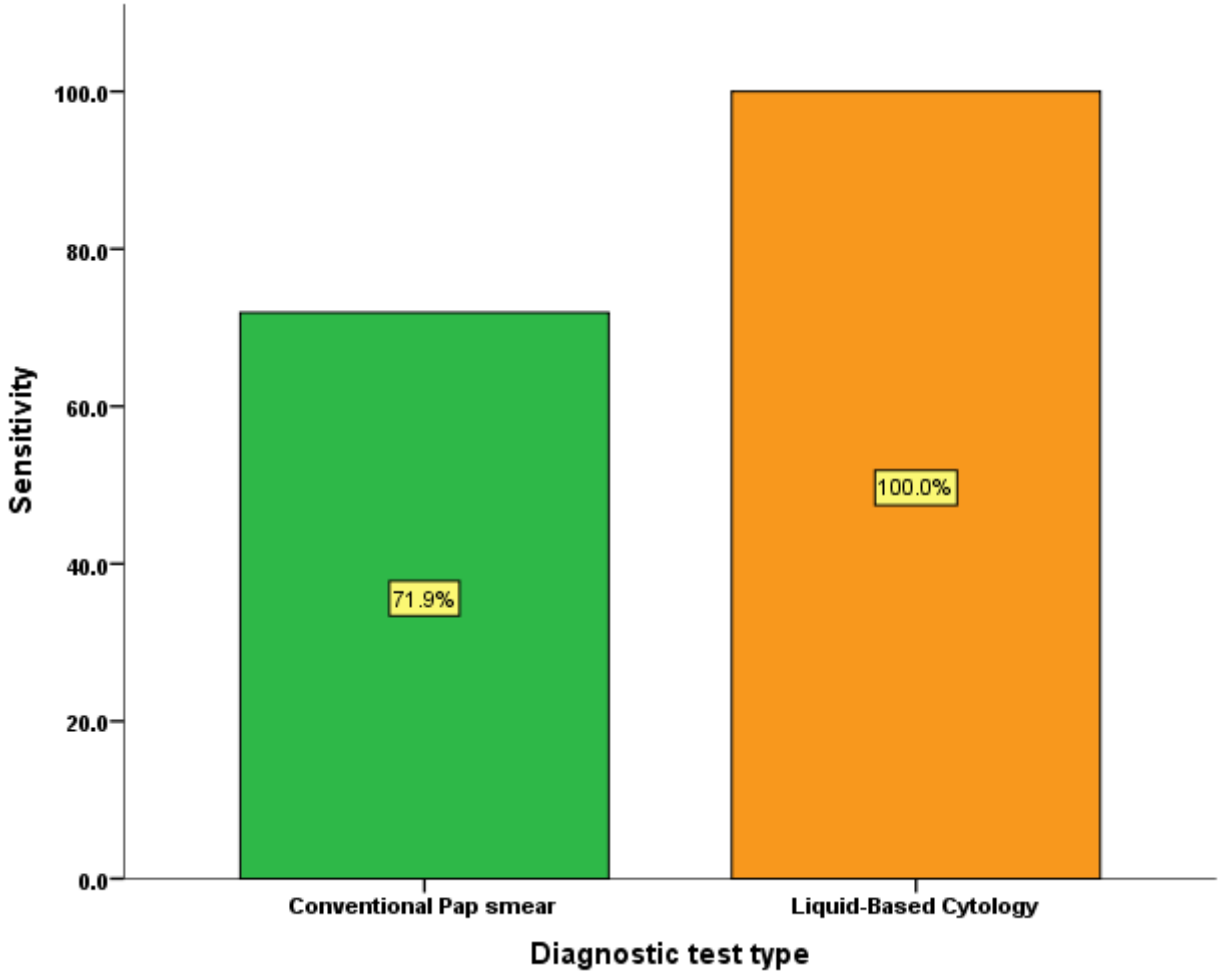

Figure 2: The sensitivity of liquid-based cytology versus conventional Pap smear methods for evaluating their effectiveness in detecting cervical cancer

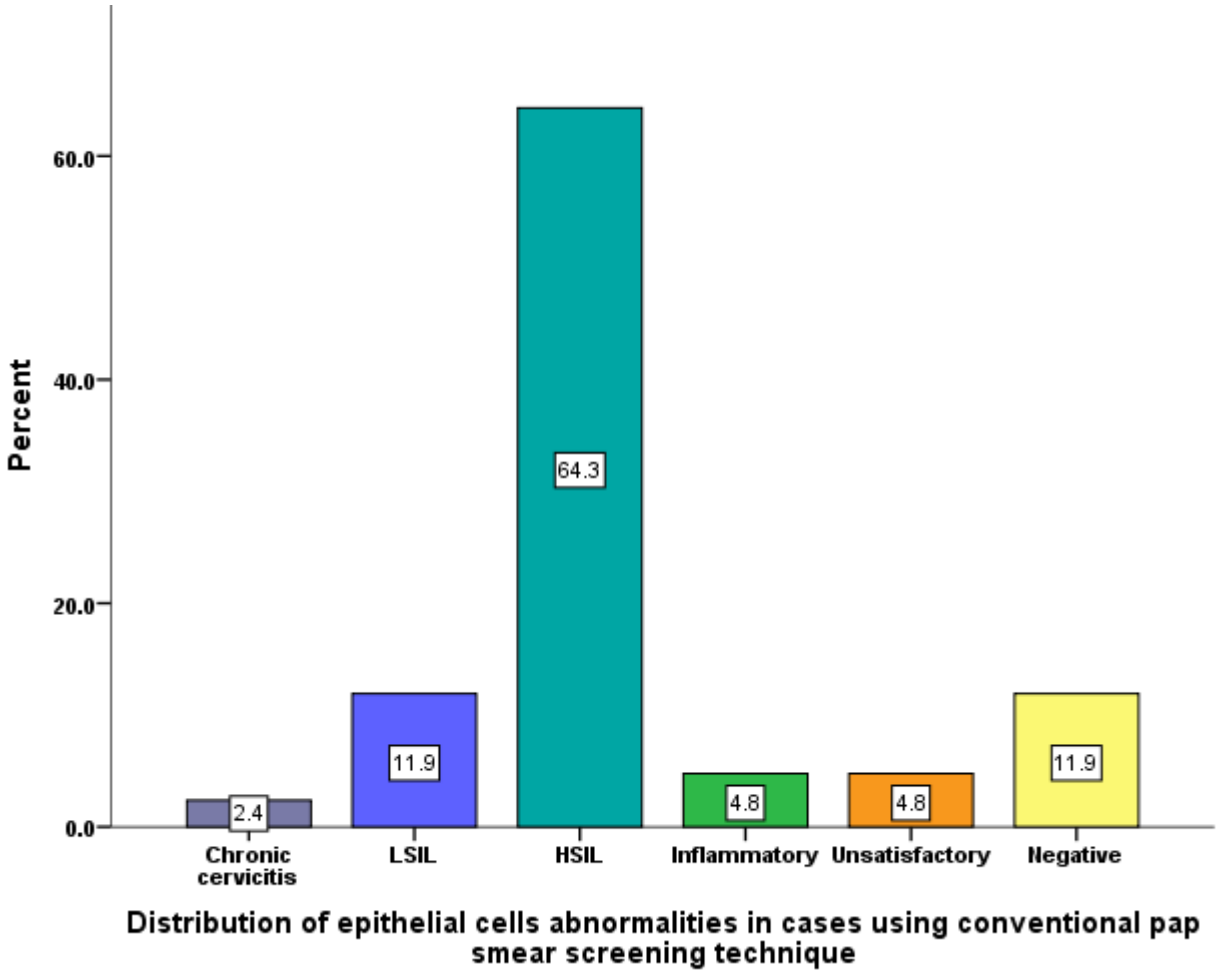

Figure 3: Distribution of cells abnormalities detected by screening method: Assesses diagnostic performance.

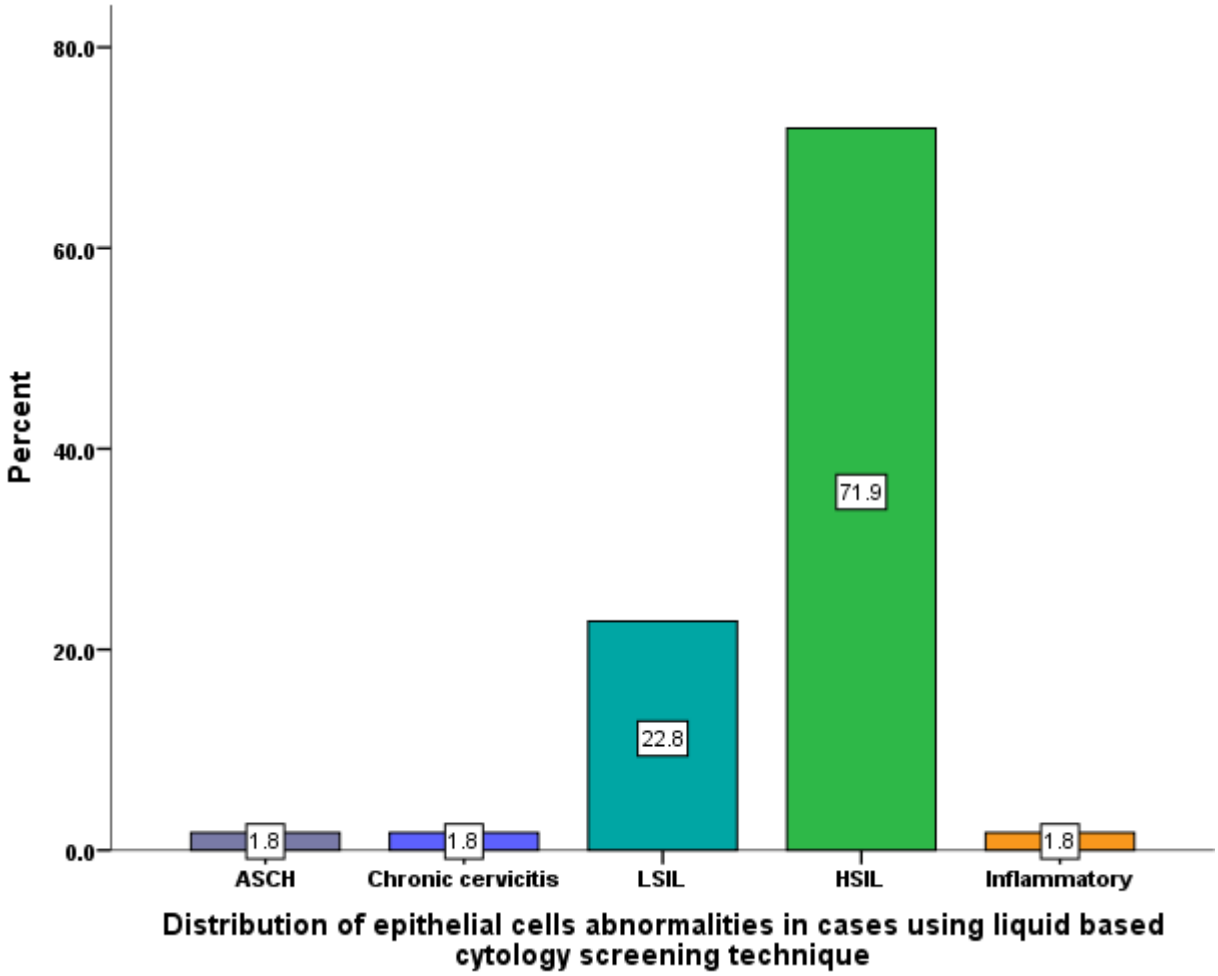

Figure 4: Distribution of cells abnormalities detected: Assesses diagnostic performance.

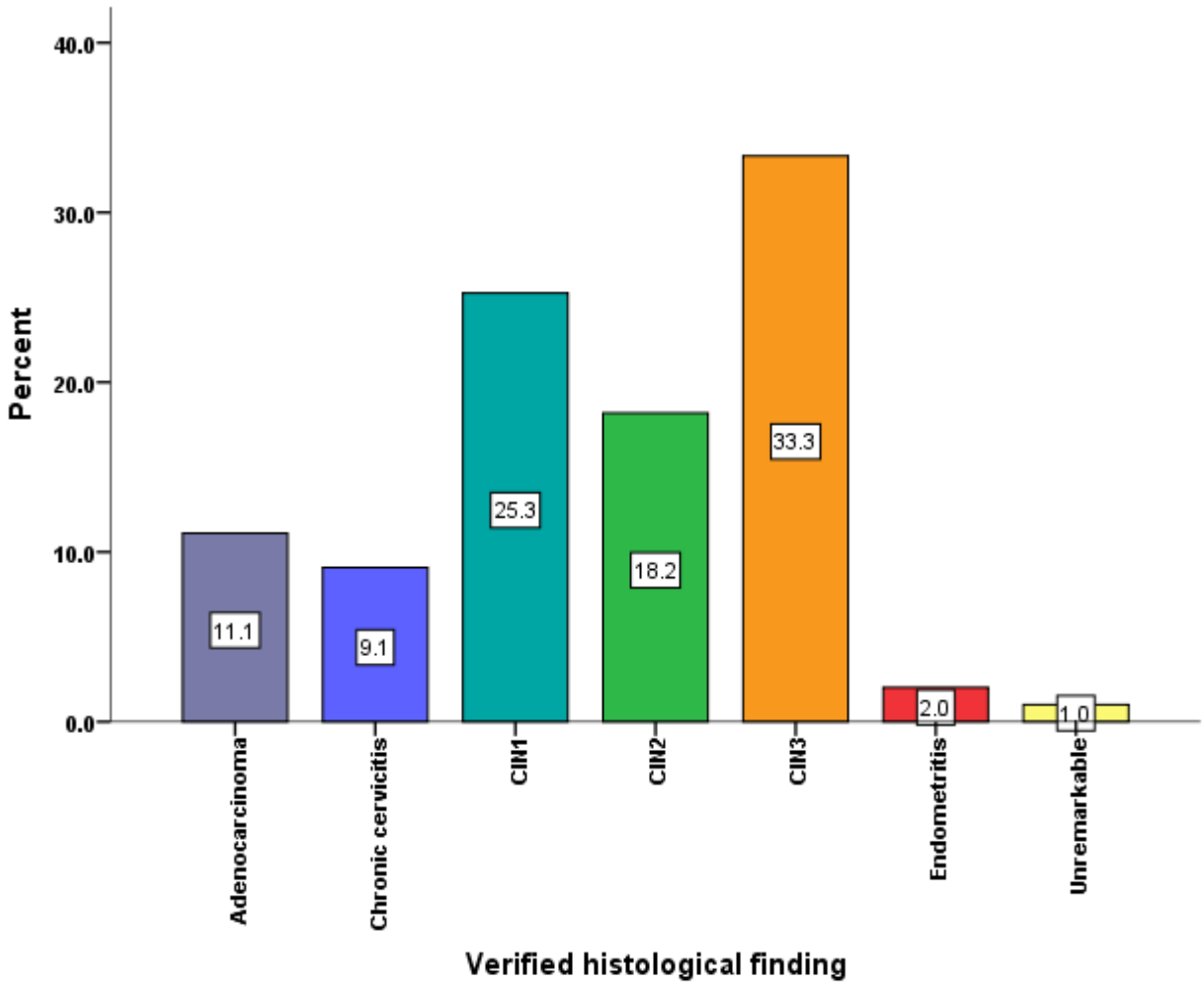

Figure 5: Verifying Histological findings with both Pap smears (Results were compared with their histology results as a gold standard)

Discussion

This study evaluated the effectiveness of liquid-based cytology (LBC) compared to conventional Pap smear in detecting cervical intraepithelial lesions among 73 patients at Ahmadu Bello Teaching Hospital (ABUTH). The mean age of presentation was 47.5 years, which is higher than anticipated when compared to other studies that reported a mean age of around 32 years. However, both ages fall within the reproductive age bracket, indicating that cervical cancer screening remains crucial in this demographic group.

A notable finding was the educational background of the participants, with 59.1% having tertiary education. This is aligned with previous studies, including Chege's work at Kenyatta University, which suggested that higher education levels are associated with greater awareness and utilization of cervical cancer screening services. Alarmingly, over 50% of participants were unaware of what a Pap smear entailed, highlighting the need for targeted awareness campaigns.

The study demonstrated that liquid-based cytology had a sensitivity of 100% for detecting both squamous and glandular lesions, significantly higher than the conventional Pap smear sensitivity of 71.9%. These findings are consistent with the findings of Uma Singh et al., reinforcing LBC's status as a more reliable

screening method. The rate of unsatisfactory results was also lower in the LBC group (1.7%) compared to conventional Pap smear (4.3%), supporting the notion that LBC offers more accurate and reliable results. Both screening methods successfully identified HSIL, with LBC detecting 71.9% and conventional Pap smear detecting 64.3% of cases. Moreover, the study revealed the prevalence of intraepithelial lesions among participants, with 51.5% having HSIL and 25.3% having LSIL, underscoring the importance of regular screening in identifying at-risk individuals.

Conclusion

The study concludes that the most common age of presentation for cervical cancer at ABUTH is 47.5 years, with an early age at menarche significantly correlating with cervical dysplasia. The results indicate that liquid-based cytology is superior to conventional Pap smear in terms of sensitivity, with a detection rate of 100% for cervical intraepithelial lesions compared to 71.9% for conventional methods. Nevertheless, both screening techniques show limitations in the detection of adenocarcinomas. LBC is therefore recommended as the preferred method for cervical cancer screening due to its higher accuracy and reliability.

Recommendations

1. Adoption of Liquid-Based Cytology: For patients with abnormal Pap smear results requiring repeat screenings, liquid-based cytology should be utilized due to its higher sensitivity compared to conventional methods.
2. Establishment of Screening Centers: Government initiatives should focus on establishing more cervical cancer screening centers in every LGA wards, emphasizing the use of liquid-based cytology to improve screening rates and outcomes.
3. Awareness Campaigns: Implementing visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) can significantly raise awareness about cervical cancer and the importance of regular screening among the general population.
4. Further Research: A prospective study should be conducted to validate these findings further and address the limitations encountered in the current study, ensuring robust recommendations for cervical cancer prevention strategies in Nigeria.

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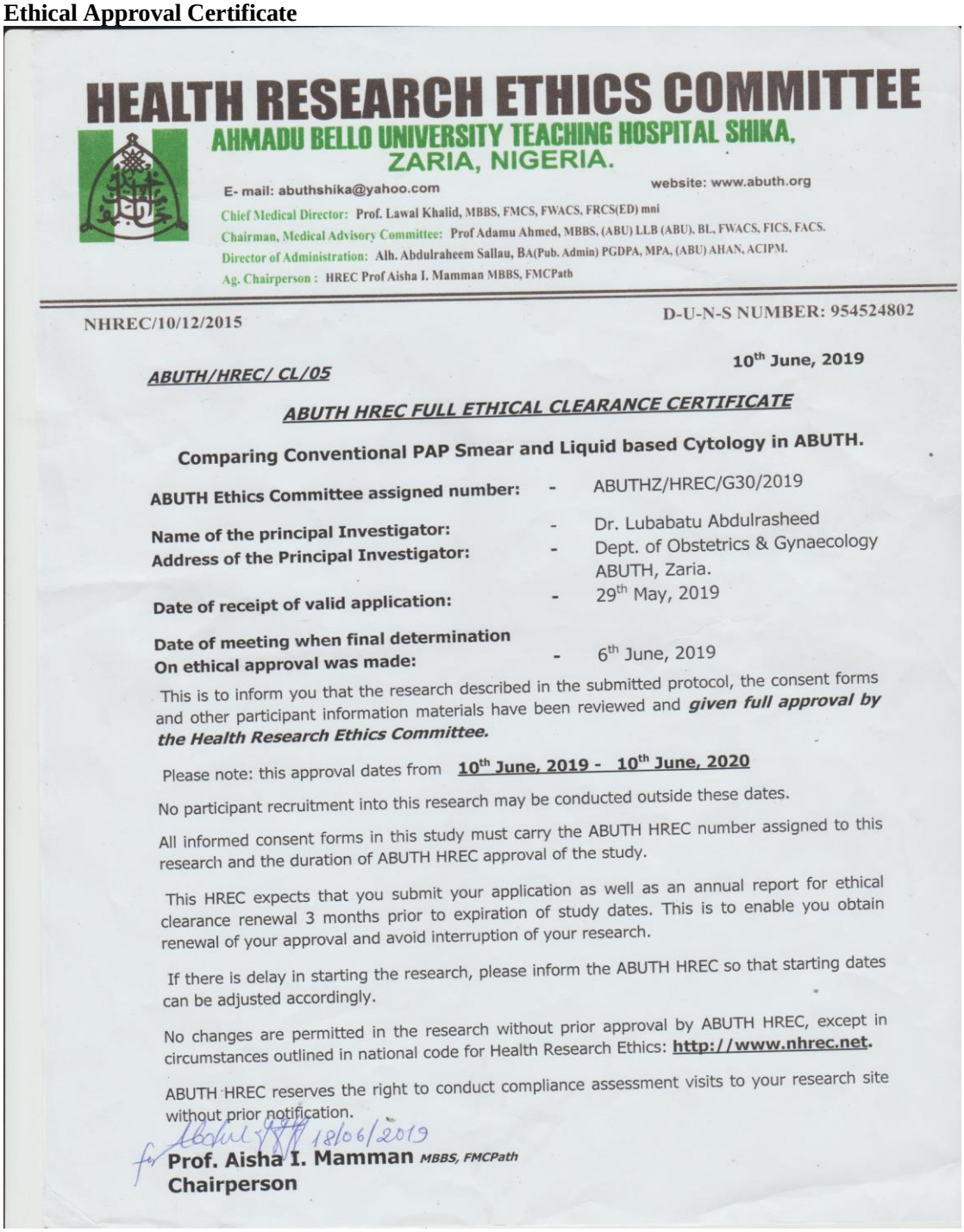
Ethical Approval Certificate



HEALTH RESEARCH ETHICS COMMITTEE

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ABUTH/HREC/ CL/05 **10th June, 2019**

ABUTH HREC FULL ETHICAL CLEARANCE CERTIFICATE

Comparing Conventional PAP Smear and Liquid based Cytology in ABUTH.

ABUTH Ethics Committee assigned number: - ABUTHZ/HREC/G30/2019

Name of the principal Investigator: - Dr. Lubabatu Abdulrasheed
Address of the Principal Investigator: - Dept. of Obstetrics & Gynaecology ABUTH, Zaria.

Date of receipt of valid application: - 29th May, 2019

Date of meeting when final determination On ethical approval was made: - 6th June, 2019

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and ***given full approval by the Health Research Ethics Committee.***

Please note: this approval dates from **10th June, 2019 - 10th June, 2020**

No participant recruitment into this research may be conducted outside these dates.

All informed consent forms in this study must carry the ABUTH HREC number assigned to this research and the duration of ABUTH HREC approval of the study.

This HREC expects that you submit your application as well as an annual report for ethical clearance renewal 3 months prior to expiration of study dates. This is to enable you obtain renewal of your approval and avoid interruption of your research.

If there is delay in starting the research, please inform the ABUTH HREC so that starting dates can be adjusted accordingly.

No changes are permitted in the research without prior approval by ABUTH HREC, except in circumstances outlined in national code for Health Research Ethics: **http://www.nhrec.net.**

ABUTH HREC reserves the right to conduct compliance assessment visits to your research site without prior notification.

for 18/06/2019
Prof. Aisha I. Mamman *MBBS, FMCPath*
Chairperson