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Cytological pattern of cervical pap smears in a teaching hospital in southern Nigeria

Aniekan Monday Abasiattai[1], Chukwuemeka Charles Nwafor[2], Ekaette Alice Tobin[3], Ntiense Maurice Utuk[1]

[1]*Department of Obstetrics/Gynaecology, University of Uyo, Nigeria*
[2]*Department of Histopathology, University of Uyo, Nigeria*
[3]*Institute of Viral and Emergent Pathogens, Irrua Specialist Teaching Hospital, Nigeria*

Abstract

Background: Cervical cancer, the most common female genital tract malignancy, remains a serious public health problem, particularly in low and middle-income countries where organized screening programs or services are either non-existent or rudimentary. Cervical cancer can be prevented by the detection and effective treatment of precursor premalignant cervical lesions.
Aim: To determine the prevalence and pattern of cervical cytological abnormalities in the University of Uyo Teaching Hospital, Nigeria.
Methods: The results of all cervical smears that were collected and processed at the Pathology Laboratory of the University of Uyo Teaching Hospital over 5 years were reviewed.
Results: A total of 497 smears were analysed. The majority of the patients were 40-49 years (35.2%). There were cervical cytological abnormalities in 11.1% of the patients, with low-grade squamous intraepithelial lesions (LGSIL) (49.1%) and high-grade squamous intraepithelial lesions (HGSILs) (18.2%) being the most predominant. About 90% of the patients with HGSILs were between 40 and 59 years, while 5.5% of the intraepithelial abnormalities were malignant.
Conclusion: The prevalence of cervical epithelial cell abnormalities in our study is relatively high, with most of the women presenting for screening late in their reproductive lives. Our findings reinforce the need for all women in our environment to begin cervical cancer screening early, and underscores the need and importance of establishing a National cervical cancer screening program to enable early detection of premalignant cervical lesions and their prompt treatment.

Key words: Pap smear, cervical screening, intraepithelial lesion, abnormal cervical epithelial cells, cervical cancer, Uyo

Introduction

Cervical cancer remains a serious public health problem, particularly in low and middle-income countries where most of the cases and deaths occur.[1] Globally, it is the fourth most common cancer in women, with around 660,000 new cases and 350,000 deaths in 2022, and about 94% of the deaths occurring in low and middle-income countries (LMICs).[2]

Well-organized screening programs, high levels of awareness, strong political will, early detection, availability of screening and treatment services, and, in recent times, vaccination programs for human papillomavirus (HPV) have all contributed to cervical cancer gradually becoming rare in most developed countries.[2,3,4] The situation is very different in LMICs, including those in Sub-Saharan Africa, where cervical cancer screening is rudimentary or non-existent, where it is the most common lower genital tract malignancy and also the most common cause of cancer-related deaths in women.[2,5] Women lose more years to cervical cancer than any other type of malignancy in the Sub-region.[2]

In Nigeria, available evidence shows that the

Corresponding Author:

Professor Aniekan Abasiattai
Department of Obstetrics/Gynaecology, University of Uyo. Nigeria

animan74@yahoo.com

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incidence of cervical cancer is about 18.4/100,000 women, with an estimated 12,075 women diagnosed every year and 7,968 deaths occurring from the disease.[2,3] It is documented to be the second most common cancer in the country.[3-5] A previous study conducted in the study center in 2004 revealed cancer of the cervix to be the most common genital tract malignancy in 49.2% of cases.[6] Unfortunately, Nigeria, as well as most other sub-Saharan African countries, does not have an established cervical cancer screening program, and screening is mostly opportunistic.[7]

Cancer of the cervix is entirely preventable because it is preceded by a long phase of pre-malignant precursor lesions that slowly undergo malignant transformation.[1,4,5] Hence, together with the easy accessibility of the cervix, this provides ample time for screening, early detection, and effective treatment of its precancerous stages.[4,8,9] It can also be effectively cured if detected in its very early stages.[1] This highlights the effectiveness of screening in reducing its incidence and associated morbidity and mortality. Unfortunately, when compared to what occurs in developed countries, women in Nigeria and indeed most other sub-Saharan countries present in very late stages of the disease (III and IV), when the prognosis is abysmal, the outcome bleak, and treatment ineffective.[4]

Cytology, HPV testing, and visual inspection are the screening strategies for identifying precancerous lesions of the cervix and preventing cervical cancer.[7] The premalignant phase of cervical cancer is detected by studying the cellular characteristics of exfoliated cervical cells.[10] To date, conventional and liquid-based cytology are the most commonly used screening methods.[5,11] While the liquid-based test is popular in developed countries, in low-resource settings such as ours, the conventional Pap smear test is the mainstay screening system.[5,12] The HPV DNA test has been shown to provide more objective results with better sensitivity and is recommended as the primary screening strategy for cervical cancer prevention; however, it is not yet readily available in Nigeria and other sub-Saharan African countries.[2]

The Papanicolaou (Pap) smear, introduced in 1941 by George Papanicolaou for the detection of precancerous changes in the cervix,[13] is widely recognized as the most cost-effective cancer screening test yet developed and has been described as the single best cancer screening procedure.[11] Exfoliated cells scraped from the surface of the squamo-columnar junction in the cervix's transformation zone are collected on a glass slide, processed, and examined microscopically for the presence of cancerous or pre-cancerous lesions.[1,5]

Since the establishment of the University of Uyo Teaching Hospital, to the best of the knowledge of the authors, no study has been conducted on the prevalence and pattern of cervical cytological abnormalities. This study was carried out to meet this need.

Materials and methods

Study design: This retrospective study was conducted at the Department of Pathology, University of Uyo Teaching Hospital (UUTH), using data collected between 1st January 2017 and 31st December 2021.

Study location: UUTH is located in Uyo, the capital city of Akwa Ibom State, in the South-South geopolitical zone of Nigeria. It is an 800-bed hospital and the only facility in the state that offers tertiary health care services. It also serves as a training institution for medical students and postgraduate resident doctors.

Study population and study procedure: The study included specimens collected from patients referred from the general outpatient clinic, the gynaecology, and the medical outpatient clinics. The cervical smears were collected in the Pathology department using an Ayre spatula and fixed immediately in 95% ethyl alcohol. A minimum of 2 slides were collected in each case and stained conventionally with Papanicolaou stain. All the stained slides were evaluated and correlated with their corresponding request cards. Information derived from the request cards included the patient's age, clinical history (indication), and referring clinic. Cytological diagnosis was made by consultants and consultants' peer group review based on the Bethesda 2014 system of reporting cervical cytology.[14] Reports without any cytological diagnosis or ambiguous diagnoses were excluded. Vault smears from patients who had undergone total hysterectomy were also excluded.

Data analysis: The extracted data from the cytology registers were analyzed using the Statistical Package for the Social Sciences version 20 incorporated Chicago, Illinois, USA. The data are presented in tables as frequencies and percentages.

Results

During the study period, a total of 497 smears were analyzed. Women aged 40-49 years accounted for the majority of cases (35.2%), followed by those aged 30-39 years (22.7%). The youngest was 19 years, while the oldest was 80 years, with a mean age of 43.34 ± 11.23 years (Table 1).

Table 2 shows the indications for the Pap smears. Screening was the most common indication (30%), followed by abnormal vaginal bleeding (18.5%), abnormal vaginal discharge (15.7%) and postcoital bleeding (10.9%).

Approximately 44.9% of the Pap smear requests originated from the General Outpatient Department (GOPD) and involved females of all age groups, except those aged 80-89 years. Requests from the Obstetrics/Gynecology department accounted for 40.4% of the cases and involved all age groups except those aged 10-19 years. A commonality between these two departments with the most requests was a similar pattern of age distribution, which is between 20-79 years. There was a steady rise from 20-29 years, peaking at 40-49 years, followed by a gradual decline. Only 19 (3.8 %) females presented via self-referrals (Table 3).

In 88.5% of cases, there was no intraepithelial lesion or malignant cell (NILM), while in 5.4% of cases, low-grade squamous epithelial (LSIL) was the diagnosis. There were three cases of squamous cell carcinoma (SCC), while atypical squamous cells of unknown significance (ASCUS) were seen in 1.6% of cases, as shown in Table 4. Among the NILM group, some associated findings included: non-specific cervicitis (25.7%), atrophic smears (13.4%), and vaginosis (4.8%).

Table 5 shows the various diagnoses in relation to the

Table 1: Age group distribution of cases

Age group (years)	Frequency	Percentage
10-19	3	0.6
20-29	58	11.7
30-39	113	22.7
40-49	175	35.2
50-59	98	19.7
60-69	34	6.8
70-79	7	1.4
80-89	1	0.2
Not recorded	8	1.6
Total	497	100

Table 2: Indications for Pap smear

Indication	Frequency	Percentage
Screening	149	30
Vaginal bleeding	92	18.5
Vaginal discharge	78	15.7
Post coital bleeding	54	10.9
Work up for surgery	16	3.2
Genital warts	11	2.2
Lower abdominal pain	10	2
Dyspareunia	9	1.8
Others	34	4.6
Not recorded	44	8.9
Total	497	100

Others include: utero-vaginal prolapse; 6, infertility work up; 5, positive visual inspection with acetic acid; 4, haematuria; 3, vulval mass; 3, weight loss; 2, vaginal itching; 2, vaginal mass; 2 and one each of the following; vaginal pain, sexual assault, peripheral neuropathy, menorrhagia, galactorrhea, secondary dysmenorrhea and left humerus metastatic adenocarcinoma

Table 3: Age group distribution of cases in relation to referral clinics N=497

Requesting clinic	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	80-89 years	Total (%)
GOPD	1	28	37	89	53	11	4	-	223 (44.9)
Gynecology	-	27	55	60	36	20	2	1	201 (40.4)
Others	2	3	21	26	9	3	1	-	65 (13.1)
Not recorded	-	1	2	2	1	1	1		
Total	3 (1.2)	59 (11.9)	115 (23.1)	177 (35.6)	99 (19.9)	35 (7.0)	8 (1.6)	1 (0.2)	497 (100)

P = 0.000. Others include: self-referral (19; 3.8%), referral from peripheral clinics (16; 3.2%), internal medicine (14; 2.8%), family planning (10; 2.1%), one referral each from a private laboratory, hematology clinic, general surgery clinic, mental health clinic, and orthopedics clinic

Table 4: Pattern of cytologic diagnoses

Cytologic diagnosis	Frequency	Percentage (%)
NILM	440	88.5
Nonspecific Cervicitis	113	25.7
Atrophy	59	11.9
Vaginosis	21	4.2
LSIL	27	5.4
HPV changes	01	
HSIL	10	2.0
ASCUS	8	1.6
AGC-NOS	5	1.0
SCC	3	0.6
ASC-H	2	0.4
Unsatisfactory	2	0.4
Total	497	100

NILM = No intraepithelial lesion or malignant cell seen, LSIL = Low grade squamous intraepithelial lesion
HSIL = High grade squamous intraepithelial lesion, SCC = Squamous cell carcinoma
ASCUS = Atypical squamous cells of unknown significance, AGC-NOS = Atypical glandular cells not otherwise specified, ASC-H = Atypical squamous cells, cannot exclude HSIL

Table 5: Age group distribution of cases in relation to cytologic diagnoses

Cytologic diagnosis	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	80-89 years	Total (%)
NILM	2	55	103	155	87	26	5	1	434
LSIL	1	1	4	9	4	5	1	-	25
HSIL	-	-	1	5	4	-	-	-	10
SCC	-	-	-	2	-	-	1	-	3
ASCUS	-	2	3	1	2	-	-	-	8
AGC	-	-	2	1	1	1	-	-	5
ASC-H	-	-	-	1	-	1	-	-	2
Unsatisfactory	-	-	-	1	-	1	-	-	2
Not recorded	-	1	2	2	1	1	1	-	8
Total	3	60	115	177	99	35	8	1	489

P = 0.065

NILM = No intraepithelial lesion or malignant cell seen, LSIL = Low-grade squamous intraepithelial lesion

HSIL = High-grade squamous intraepithelial lesion, SCC = Squamous cell carcinoma

ASCUS = Atypical squamous cells of unknown significance, AGC-NOS = Atypical glandular cells not otherwise specified, ASC-H = Atypical squamous cells, cannot exclude HSIL

age groups. NILM was seen in all age groups with a steady rise through the age groups, peaking at 40-49 years, followed by a steady decline. LSIL was seen in all age groups except those aged 80-89 years and had almost a similar pattern to those with NILM. There is no significant association between the diagnoses and the age groups.

Discussion

The prevalence of cervical cytological abnormalities in our study was 11.5%. The majority of patients were between 40 and 49 years, screening was the most common indication for the Pap smear, and low-grade squamous intraepithelial lesion (LGSIL), the most frequent intraepithelial abnormality.

The mean age of the patients in our study is similar to the findings from studies conducted by Duru et al[3] in Owerri, Nigeria, Akinfolarin et al[1] in South-western Nigeria, and Odusolu et al[15] in Calabar, Nigeria. It is, however, lower than the findings of a study by Bakari et al,[10] where the largest number of women were between 35-44 years. This implies that women in our environment are screened for cervical cancer or referred for screening in the later parts of their reproductive life. This may have far-fetched adverse consequences, when considering the need to identify cervical premalignant cells early in order to institute prompt and effective treatment and prevent progression to invasive cancer, taking into consideration that it typically takes about 15 years (10-20 years) for cervical cancer to develop from its precancerous stages.[17]

In a bid to ensure premalignant lesions are identified early, most guidelines recommend that screening for cervical cancer begin as early as possible. The Society of Gynaecologists and Obstetricians of Nigeria (SOGON)[7], recommends screening from the age of 25 years for low-risk women and below this age for those at high risk. The World Health Organization (WHO)[17] recommends regular cervical cancer screening from 30 years for the general population and from 25 years for those who are HIV-positive, while the American College of Obstetricians and Gynaecologists (ACOG), in their latest update[18], recommends that screening start at 21 years.

The prevalence of intraepithelial abnormalities in our study (11.5%) is similar to reports from studies conducted in Jos[12] and Yola (12.1%)[10] Nigeria, but lower than the 16.3% reported from Calabar, Nigeria.[15] Our figure, however, is higher than the 6.4% and 6.8% reported from Owerri[5] and Sokoto[19], both in Nigeria, respectively. These figures are similar to those from low and medium-income countries in Asia, where prevalences of between 3.8% - 8.5% have been reported.[8,11,20,21]

Factors documented to be responsible for this wide range of prevalence rates include cultural differences, age at screening, awareness of screening, and presence or absence of cervical cancer screening programs.[21] Others include intrinsic differences in the population studied, prevalence of risk factors, and sample size.[22] The relatively high prevalence of intraepithelial abnormalities in our center underscores the importance of ensuring that as much as possible, our women avail themselves of screening to benefit from its primary preventive effect.

Low-grade squamous intraepithelial lesion (LGSIL) was the most common premalignant cervical abnormality in our study population. This appears to be the trend in most Nigerian studies[1,10] and indeed studies from other parts of the world.[22] LGSIL are morphological correlates of HPV infection.[23] They are characterized by a shorter and less observable clinical course, and may spontaneously regress in a significant proportion of patients.[10]

High-grade squamous intraepithelial lesions were identified in 2.0% of the study population, with about 90% of those affected being between 40 and 59 years. This figure is higher than the 0.49% reported by Nair et al[22], the 0.6% reported by Arul[20], and 0.48%

reported by Sachan et al[8], all in Asia. This high prevalence of HGSIL in our setting is not surprising, considering the high prevalence of cancer of the cervix in our state, which has been revealed in previous studies.[6,24] HGSIL are morphological correlates of cervical precancers[23], and available evidence[25] shows that if not treated, approximately 31% to 50% of affected patients will progress to cancer within 30 years.

The smears of three patients (5.5% of the intraepithelial abnormalities) revealed malignant epithelial cells, which were all squamous cell carcinomas, and 2 (90%) of these were in women aged 40-49 years. These results are similar to those from Calabar, Nigeria[15] where the majority of those with malignant epithelial cells were of the same age bracket, but higher than the figures from countries in Asia[20,21], where the proportion of women with malignant epithelial cells were fewer, and in one study out of 1650 women sampled, none had malignant epithelial cells.[8] This high prevalence of malignant epithelial cells among our women, when compared to the Asians, may not be unconnected with the much higher prevalence of HIV in our setting[26]. Squamous cell carcinoma is documented to be responsible for over 90% of cancers of the uterine cervix[24]. Considering that most of our patients present in very late stages with associated high morbidity and mortality, and also, the long time it takes for invasive cancer to develop from cervical intraepithelial lesions, and the high prevalence of HIV in our state from sentinel surveys over the years, our women should start cervical screening very early, probably as recommended by the ACOG.[18]

The most common presenting symptom was vaginal bleeding, followed by an abnormal vaginal discharge, then postcoital bleeding. This aligns with reports from Owerri[5], and this is probably because over 80% of the patients were referred from the gynaecology clinic and the general outpatient department. Since there is no organized cervical cancer screening program in Nigeria, clinicians seize the opportunity to screen or refer patients for cervical cancer screening when they generally present to the hospital.

In addition to detecting pre-malignant cells, cervical cytology has the benefit of identifying cervico-vaginal microorganisms responsible for vaginal infections enabling effective treatment. Bacterial vaginosis (BV) a vaginal dysbiosis characterized by a shift in the vaginal biodata from protective lactobacilli species to facultative -anerobic bacteria and strict anerobic bacteria,[27] was the most common aetiology identified in inflammatory smears. If left untreated, BV can lead to serious reproductive health outcomes, which include an increased risk of preterm labour, preterm rupture of membranes, low birth weight, sexually transmitted infections including HIV, pelvic inflammatory disease, puerperal sepsis and postoperative complications such as vaginal cuff cellulitis.[28]

Limitations

This study was carried out in a tertiary hospital; hence, it may not be representative of what is obtainable in the general community. Due to the study's retrospective design, patients with epithelial cell abnormalities were not followed up to assess management outcome. Some request cards contained incomplete information, which may have resulted in inconsistencies in analysis. However, the results emphasize the need for all women to avail themselves of cervical cancer screening.

Conclusion: The prevalence of cervical epithelial cell abnormalities in our study was relatively high, with most of the women presenting for screening late in their reproductive lives. Our findings reinforce the need for all women in our environment to begin cervical cancer screening early, and underscores the need and importance of establishing a National cervical cancer screening program to enable women access cervical screening services, which should ultimately result in early detection of premalignant cervical lesions and their prompt treatment.

Conflict of interest: None

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