Histopathological study of surgical cervical biopsies in Lagos, Nigeria

Francis A. Faduyile, Sunday S. Soyemi, Kikelomo O. Wright, Fadesewa I. Osuolale[1]

Departments of Pathology and Forensic Medicine, [1]Community Health and Primary Health Care, Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria

ABSTRACT

Introduction: Benign lesions of the cervix such as hyperplasia, endometriosis, cervicitis and endocervical polyps are health concerns for women globally. Meanwhile, Cervical cancer is the fourth most common cancer among women in the world, with developing countries bearing the brunt of the burden in terms of morbidity and mortality. This study examines the histopathological pattern of cervical biopsies in a tertiary health institution in Lagos, Nigeria.

Materials and Methods: This was a retrospective study of all cervical biopsies received in a government-owned tertiary health institution and a private pathology laboratory both in Ikeja over an 8-year period. All the slides were retrieved and reviewed while socio-demographic and clinical details were obtained from request and clinical notes. Data analysis was conducted using the Statistical Package for Social Science version 20.

Results: A total of 901 biopsies were retrieved, representing 4.8% of the total biopsies conducted. The age range of patients was 19–87 years with a mean age of 49 ± 13.0 years. The benign tumours accounted for 58.8% of the cases, with a benign to malignant ratio of 1.5:1. Squamous cell carcinoma (SCC), endocervical polyps, and cervical intraepithelial neoplasm accounted for 36.1%, 30.9%, and 15.1% of the total cervical biopsies, respectively. The benign tumours were statistically related to the younger age groups ($P = 0.00$), however, malignant tumours showed no relationship with age group ($P = 0.325$).

Conclusion: SCC and endocervical polyps were the most common malignant and benign cervical biopsies, respectively. The benign tumours were seen more in the younger age group. Early detection of some of these benign conditions may provide an opportunity for appropriate interventions to prevent further complications.

Key words: Benign; biopsy; cervical cancer; cervical intraepithelial neoplasm; endocervical polyps; malignant; squamous cell carcinoma.

Introduction

The cervix is the most inferior portion of the uterus, which protrudes into the upper vagina.[1] Being the gateway into the womb, it is prone to infections and other pathological conditions such as cancer, hyperplasia, endometriosis, cervicitis, and endocervical polyps.[2] Chronic non-specific cervicitis is the most common inflammatory lesion with variable aetiological microbial agents.[3] The prevalence rate of cervicitis among other non-neoplastic lesions of the cervix in Nigeria has been reported by two separate studies to be 59.8% and 80.0%, respectively.[4,5]

Benign lesions of the cervix are common and include endocervical hyperplasia, endometriosis, Nabothian cysts,

Address for correspondence: Dr. Francis A. Faduyile, Department of Pathology and Forensic Medicine, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. E-mail: abaaye@yahoo.com

and endocervical polyps.[6] Nwachokor and Forae documented 56.3% of cervical lesions as benign with a benign to malignant ratio of 1.3:1.[4] Other studies have also reported that endocervical polyps is one of the most frequent benign lesions in the cervix, with rates ranging between 60.0% and 91.7%.[4,7,8]

Cervical cancer is the fourth most common cancer among women in the world. In 2012 alone, 528,000 new cases were detected globally.[1] Eighty-five percent of cervical cancer global burden occurs in the developing countries, and 90% of cervical cancer deaths also occur in these regions.[1] Nnadi *et al.* studied gynaecologic malignancies in northern Nigeria observing that cervical cancer is the most common gynecological malignancy.[9]

Early diagnosis of cervical lesions is vital for the reduction of the burden of ill health associated with these conditions. Furthermore, an understanding of cervical disease pattern is essential for programmatic decision on how best to manage and plan for appropriate interventions in promoting maternal health. The goal of this study is to determine the histopathologic pattern of cervical biopsies in a private and a tertiary health institution in Lagos, Nigeria.

Materials and Methods

This is a retrospective study of all cervical biopsies received in a government-owned tertiary health institution and a private pathology laboratory both based in Ikeja, Lagos, Nigeria over an 8-year period between 1st January 2008 and 31st December 2015. The tertiary pathology laboratory serves as the teaching hospital with over thirty secondary health care facilities in Lagos State with a population of over 15 million people. It also serves as a referral centre to patients from the contiguous states in the country. The private laboratory serves mainly the private hospitals in Ikeja area and its immediate environs. Approval for the use of data was obtained from the department of Pathology and Forensic Medicine, LASUTH, and the management of the private pathology laboratory.

All the formalin-fixed paraffin-embedded (FFPE) slides were retrieved and reviewed by first two authors. In cases of broken and lost slides, sections were re-cut from the block, stained with routine haematoxylin and eosin stains (H and E) and examined microscopically.

The demographic and clinical information were obtained from request forms, and where applicable the clinical notes were sought. The data were analysed using the Statistical Package for Social Science version 20, as presented in tables

and figures. Chi-square was used to test the association between variables, and statistical significance was taken as *P* value < 0.05.

Results

A total of 901 cervical biopsies were received out of the total of 18745 biopsies during the period under review, representing 4.8% of the total biopsy received. The mean age was 49 ± 13.0 years with an age range of 19 to 87 years.

Most of the cervical biopsies were from patients in the 5th decade of life, followed by patients in the 31–40 years age group. Most (58.8%) of the biopsies were benign with a benign to malignant ratio of 1.5:1 [Table 1].

Table 2 revealed that endocervical polyps accounted for 51.1% of the total benign lesions seen and this was followed by cervical intraepithelial neoplasm (CIN) (24.9%). Squamous cell carcinoma (SCC) accounted for 36.1% of the total cervical biopsies studied. The others included Nabothian cysts, adenomyosis, and cervical prolapse among others.

Table 1: Demographic profile

Parameter	Frequency	Percentage
Age category (years)		
Below 30	34	3.8
31-40	250	27.7
41-50	286	31.7
51-60	169	18.8
61-70	106	11.8
Above 70	56	6.2
Diagnosis		
Benign	530	58.8
Malignant	344	38.2
Insufficient	27	3.0

Table 2: Histopathological diagnosis of cervical biopsies

Parameter	Frequency	Percentage	Percentage total
Benign			
Adenomyosis	8	1.5	0.9
Cervicitis	91	17.2	10.4
Cervical intraepithelial neoplasia (CIN)	132	24.9	15.1
Granular cell tumour	3	0.6	0.3
Endocervical/leiomyomatous polyp	271	51.1	30.9
Others	25	4.7	2.8
Total	530	100.0	
Malignant			
Adenocarcinoma	20	5.8	2.3
Poorly-differentiated carcinoma	7	2.0	0.8
Squamous cell carcinoma (SCC)	317	92.2	36.1
Total	344	100.0	100.0
	874		

CIN accounted for approximately half of all premalignant lesions (46.2%) and only about one-fifth of CIN were in the high grade. Most of the SCC was well-differentiated (keratinising) as against only a quarter non-keratinising [Table 3].

There was a steady rise in the proportion of malignant lesions compared to benign lesions until it became the predominant diagnosis from the 6th decade of life. The classification (benign or malignant) in relation to patient age was statistically significant [Figure 1].

Most of the benign tumours and inflammatory conditions occurred in the 4th and 5th decade of life and there was a decline from the 6th decade of life. A statistically significant association was also observed between the diagnosis of benign tumours and patients' age [Table 4].
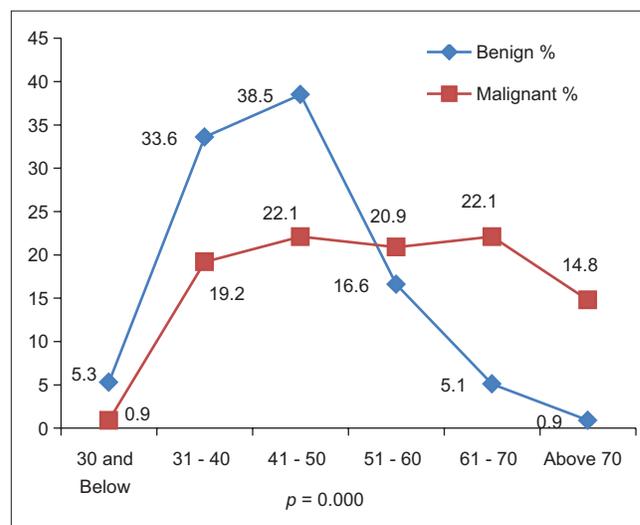
There was a similarity in the proportion of SCC within the age groups with the 7th decade being the highest. Adenocarcinoma was most common in the 6th decade followed by the 5th decade. There was, however, no significant association between the age and the time/decade of diagnosis of malignancy [Table 5].

Discussion

The proportion of cervical biopsies to the total biopsies of 4.8% observed in this study is slightly higher than the 3%

Table 3: Pre-malignant lesions and differentiation of SCC

Parameter	Frequency	Percentage
Cervical intraepithelial neoplasia		
1	61	46.2
2	43	32.6
3	28	21.2
Total	132	100.0
Squamous cell carcinoma		
Keratinising	258	81.4
Non-keratinising	59	18.6
Total	317	100.0

Figure 1: Graph showing the diagnosis in relation with the age group

Table 4: Cross-tabulation of benign lesions against age groups

Age (years)	Adenomyosis	Cervicitis	CIN	Granular cell tumour	Endocervical polyp	Others	Total
30 and below	3 (37.5%)	5 (5.5%)	3 (2.3%)	-	17 (5.7%)	-	28 (5.3%)
31-40	3 (37.5%)	29 (31.9%)	48 (36.4%)	3 (100.0%)	124 (41.2%)	2 (8.0%)	178 (33.6%)
41-50	2 (25.0%)	37 (40.7%)	60 (45.5%)	-	94 (31.2%)	10 (40.0%)	204 (38.5%)
51-60	-	15 (16.5%)	12 (9.1%)	-	55 (18.3%)	6 (24.0%)	88 (16.6%)
61-70	-	3 (3.3%)	6 (4.5%)	-	11 (3.6%)	7 (28.0%)	27 (5.1%)
Above 70	-	2 (2.2%)	2 (2.3%)	-	-	-	5 (0.9%)
Total	8 (100.0%)	91 (100.0%)	132 (100.0%)	3 (100.0%)	301 (100.0%)	25 (100.0%)	530 (100.0%)

P=0.000

Table 5: Cross tabulation of malignant tumour against age groups

Age (years)	Adenocarcinoma	Poorly-differentiated carcinoma	Squamous cell carcinoma	Total
30 and below	-	-	3 (0.9%)	3 (0.9%)
31-40	2 (10.0%)	-	64 (20.2%)	66 (19.2%)
41-50	6 (30.0%)	2 (28.6%)	68 (21.5%)	76 (22.1%)
51–60	7 (35.0%)	-	65 (20.5%)	72 (20.9%)
61-70	3 (15.0%)	2 (28.6%)	71 (22.4%)	76 (22.1%)
Above 70	2 (10.0%)	3 (42.8%)	46 (14.5%)	51 (14.8%)
Total	20 (100.0%)	7 (100.0%)	317 (100.0%)	344 (100.0%)

P=0.325

seen by Omoniyi-Esan *et al*. in a similar study conducted in south-west Nigeria.[5] The benign to malignant tumour ratio of 1.5:1 seen in this study is consistent with other related studies, which have reported preponderance of benign tumours and ratio of 1.3:1.[4,10]

Among benign cases, endocervical polyp was the most common diagnosis, which represented over one-half of the total benign diagnosis and 31% of the total cervical biopsies received. The preponderance of endocervical polyp among the benign lesions is in consonance with other studies with rates varying from 60.0% to 91.7%.[4,7] This may also be related to the higher prevalence of leiomyoma among women of African decent. Cervicitis, an inflammatory disease comprising acute cervicitis and chronic non-specific cervicitis, accounted for a quarter of all benign tumours and 10% of all cervical biopsies received in this study. Most cases of cervicitis are often due to non-specific causes or infective agents.[4] Omoniyi-Esan *et al*. in a study on non-neoplastic diseases of the cervix showed a prevalence rate of 82% of chronic non-specific cervicitis out of 37.5% of all cervical surgical biopsies.[5] The higher prevalence rate in that study may be as a result of the addition of other tumours apart from the inflammatory cases.[5] This study also showed a drop in the diagnosis of benign diseases with advancing age of the patients, which was statistically significant.

CIN, which is a premalignant lesion, was seen in 15% of all cervical biopsies received with the prevalence of CIN 1, 2, and 3 of 46.2%, 32.6% and 21.2% respectively. There was a reduction in the prevalence of CIN from the low-grade CIN to high-grade CIN. The mean age of patients with the low grade CINs (1 and 2) was 44 ± 10 years whereas the mean age of CIN 3 was 48 ± 9 years. These findings are believed to be because of the higher rate of human papilloma virus (HPV) infections, the causative agents of CIN, in the younger age group and the clearing of the infection in the older age group.[11] The lower prevalence of the higher grade of CIN can also be explained by the body's natural immune response in clearing such infections.[11]

Among the malignant tumours, SCC accounted for 92.2% and was also the most common diagnosis (36%) of all cervical surgical biopsies in this study. Several Nigerian studies showed an SCC prevalence rate between 88.0% and 93.9% among malignant tumours.[12-15] This high rate of SCC in Nigeria could reflect the low uptake of the Pap test and other screening measures such as visual inspection with acetic acid (VIA) capable of identifying dysplastic conditions before transformation to malignancy. SCC of the cervix has been reduced drastically in many developed countries as a result of organised cervical screening with Pap test and HPV vaccination.[16]

Most of the SCC (81.4%) in this study were well differentiated (keratinising) as against the non-keratinising variants. Similar studies by Adelusi *et al*. from Ibadan and Adeniji from Ilorin found a well-differentiated SCC prevalence of approximately 60.1%.[15,16] This finding is, however, at variance with that of Abdus-salam who reported that 53.4% of the SCC tumours were poorly differentiated, 14% moderately differentiated, and 32.6% well differentiated.[12] Adeniji also observed that patients above the age of 45 years had well differentiated SCC.[17] Although the various methods of histologic grading have not been found to have any significant impact on prognosis.[18,19]

Olu-Eddo *et al*. also found an age range for cervical cancer as 15–90 years with a mean age of 50.4 years (SD $\pm$ 13.5) and a peak occurrence in the 5th decade.[13] Adeniji reported an age range of 23–85 years with peak age at 5th and 7th decade and average age of 51.8 years.[17] This study, however, showed a fairly equal distribution of SCC from the 3rd to the 7th decade, with a mean age of 55 ± 14 years and age range of 24–87 years, which is closely related to the observation of Adeniji and Olu Eddo *et al*.[13,17]

Adenocarcinoma and poorly-differentiated (unclassified) carcinoma were 5.8% and 2.0%, respectively, of the total malignant diagnosis. The low prevalence of adenocarcinoma seen in this study is consistent with other studies in Nigeria which range between 2.4% and 12%.[12-15,17]

We also found out that, with advancing age, the rate of cancer diagnosis increased and it became the dominant diagnosis of cervical biopsies from the 6th decade of life, although there was no statistical significance between the age of patients and diagnosis of malignancy. However, there was a statistical significant relationship between the diagnosis of benign tumours and age of patients. The diagnosis of benign tumours reduced with advancing age.

The limitation of this study being a retrospective one includes our inability to extract details like if the tumours were diagnosed by screening or by symptoms, presence or absence of patient's co-morbidities, our inability to properly follow up the CINs to determine if there was progression or retrogression of the disease amongst others.

Conclusion

SCC was the most common diagnosis of cervical biopsies and were mainly well-differentiated type. Endocervical polyp was

the most common benign tumour in cervical biopsies. The age of patients was statistically significant with the diagnosis of benign diseases but not with malignant conditions. Cervical biopsies from the 6th decade of life are more likely malignant. Early detection of some of these benign conditions may provide an opportunity for appropriate interventions to prevent further complications such as progression from benign to malignant conditions.

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Conflicts of interest
There are no conflicts of interest.

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