Research Article

Histopathological Evaluation of Cervical Lesions in Tertiary Based Hospital with Review of Literatures

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Abstract

Background: This is the first base line retrospective study to review morphology of different patterns of cervical lesions in Histopathology department, Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi since the institution of the hospital. **Aims:** This research is aimed at reviewing all cervical lesions in the department of Histopathology NAUTH, Nnewi. **Methods:** The pathology report forms in histopathology department were retrieved and relevant information such as age, histologic number, specimen sites, type of surgery, clinical and histological diagnosis were extracted. A total of 166 cases of cervical lesions were obtained within the 5-year study period of which 160 cases fulfilled inclusion criteria and therefore were analysed. The processed tissue and the slides stained with regular histochemical stain (Haematoxylin and eosin) technique in this study period were reviewed by the above researchers using multi-headed microscope (®CARL ZEISS). Cervical tumours seen were classified according to the World Health Organization (WHO) tumour book (edition 2020). **Results:** Of these 160 cases, 89 were malignant, 17 were benign tumours and tumour-like lesions, 34 were premalignant lesions while 20 cases were non-neoplastic lesions. The malignant cervical lesions were far more common & accounted for 55.6% of the entire cervical lesions, of which 83 cases (51.9%) were invasive Squamous Cell Carcinoma (SCC). The second commonest malignancy was adenocarcinomas with just 6 cases (3.75%). Among these invasive SCC, large cell non-keratinising variants predominate with 39 cases (24.4%) followed by large cell keratinising SCC with 34cases (21.3%) and 6 cases (3.8%) of small cell non-keratinizing SCC, while clear cell SCC were just 3 cases (1.88%). In premalignant lesions, High Grade Squamous Intraepithelial Lesions (HSIL) were commonest with 27 cases (16.9%) which included CIN2:15 cases (9.4%) and CIN3:12 cases (7.5%) making High Grade Squamous Intraepithelial Neoplasm (HSIL) far higher than Low Grade Intraepithelial Lesion (LSIL or CIN1) which were just 7 cases (4.4%). In benign-neoplastic lesions or tumour-like lesions; endometrial polyp were 7 cases (4.4%) making it the commonest benign lesion followed by benign epithelial lesion of which Squamous metaplasia and Nabothian cyst were 4 cases each (2.5%) while cervical Leiomyomatous polyp were 2 cases with a frequency of 1.25%. In non-neoplastic cases, all the lesions were inflammatory with chronic non-specific cervicitis being the commonest with 19 cases (11.9%) of which 12 cases occurred in UV-prolapse followed by one case of plasma cell granuloma (0.6%). The mean age of cervical cancer as observed by this index study was 57.76 ± SD 12.63 which correspond with the mean ages of high grade squamous intraepithelial neoplasm; CIN3 & CIN2 having 59.92 ± SD 11.74 and 60.20 ± SD 11.21 respectively. **Conclusion:** Invasive cervical SCC is quite common in our environment with an alarming rate of its premalignant lesion (HSIL). There is need for continuous cervical screening exercise among sexually active young females and the need for government to implement preventive measures such as HPV vaccine as routine immunization plan for every born Nigerian male and female to eliminate these premalignant lesions.

Keywords: Invasive SCC; Endocervical adenocarcinoma; HSIL; Chronic Non-specific cervicitis; Endocervicalpolyp

Introduction

The majority of specimens in the histopathology department were gynecological cases. The uterine cervix is prone to develop several no neoplastic and neoplastic lesions. These lesions are most commonly seen in sexually active women. Majority of the no neoplastic lesions are inflammatory in nature. [1] However,

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most literatures report that the second most common lesion of the cervix is cervical malignancies.

Cervix is an important tube-like bulbous fibrous organ in female that separates the lower and upper genital tract and is divided histologically into "endo" and "ecto" cervix joined together by transformation zone. This zone is subject to hormonal changes, and is also a focus for premalignant and cancer development. [2]

Cancer is responsible for about 51 million deaths yearly, out of which cervical cancer accounts for 8.5%, most of which occurred in the developing countries. [3] Cervical cancer is the most common cancer of female genital tract in most low-income countries but ranked as the second most common cancer after breast cancer among women worldwide. About half a million new cases are seen worldwide each year, most occurring in developing countries. [3] The incidence and mortality rates are high in Africa and some parts of Asia, and are low in Australasia and West Asia; it has however declined substantially in the Western countries following the introduction of intensive cervical screening program and availability of HPV vaccines. [4]

Cervical cancer has a strong association with infection of Human Papillomavirus especially human papillomavirus type 16 and human papillomavirus type 18 infections, which jointly cause 70%–75% of all cervical cancers and 40%–60% of its precursors.[5] Cervical cancer assumed even greater prominence with increase in the incidence of HIV/AIDS infections which are still ravaging in the developing world. The work of Muñoz et al. has also shown other contributing factors to cervical cancers which include tobacco smoking, high parity, long-term hormonal contraceptive use, co-infection with Chlamydia trachomatis, multiple sexual partners, herpes simplex virus type 2, immunosuppression, certain dietary deficiencies, and genetic and immunological host factors. [5]

The cancer of the cervix is preceded during 10 to 15 years by precancerous lesions caused by HPV 16 and 18 characterized by atypical changes (dysplasia) of the cells in the transformation zone. Cervical dysplasia occurs at 1% to 5% of the women in the general population. It is significantly a health problem globally. It affects primarily the young and the old women from 25 to 35 years. [6] It is classified into two tier grading system; Low Grade Intraepithelial Lesion (LSIL) and High-Grade Intraepithelial Lesion (HSIL) with HSIL being more likely to progress to cervical cancer. Studies recently conducted in Côte d'Ivoire and Nigeria found the prevalence of precancerous cervical cancer lesion to be 11% and 6% respectively. [7] It is estimated that each year, approximately 69,000 new cases of dysplasia of low rank and 15,000 cases of dysplasia of high rank are seen in Europe. [8]

Other cervical lesions include benign-tumour and tumour-like cases. The commonest benign tumor of the cervix is endocervicalpolyp, others include Nabothian cyst, and cervical leiomyomas. Leiomyomas of the cervix are rare and may be clinically mistaken for malignancy. [2]

Therefore, this research is aimed at showing our histologic documentations on cervical lesions and also to compare these data with local and international studies.

Materials and Methods

The pathology request forms of all cases of gynaecological lesions seen at the Histopathology department of Nnamdi Azikiwe University Teaching Hospital, Nnewi for 5 years starting from January 2010 to December 2014 were retrieved. The demographic information such as clinical bio-data, anatomical site, clinical diagnosis and nature of specimens which include incisional biopsies, cone biopsies, and total abdominal hysterectomies were extracted. A total of 923 cases were obtained but only 160 cases (17.33%) that fulfilled inclusion criteria as cervical lesions were analyzed. The processed tissues and the slides stained with regular histochemical stain (Haematoxylin and eosin) technique were reviewed by above researchers using multi-headed light microscope (®CARL ZEISS). Cervical tumors seen were classified according to the World Health Organization (WHO) tumour book (edition 2020). Data were entered using Micro-soft Excel package and transferred to statistics software (Statistical Package for the Social Sciences version 21, SPSS Incorporated, Chicago, Illinois, USA) for descriptive analysis. The cases were analyzed using simple SPSS statistical tables, pie charts and histograms.

Results

A total of 923 gynecological cases were obtained but only 160 cases (17.33%) that fulfilled inclusion criteria as cervical lesions were studied. Of these 160 cases, 89 (55.6%) were malignant, 34 (21.25%) were premalignant lesions; benign lesions were 37 (23.13%) of which 17 cases were benign tumour or tumour-like lesions, while 20 cases were non-neoplastic lesions. Out of these 160 cervical lesions received, 137 patients (85.6%) had hysterectomy whereas 23 patients (14.4%) had cervical biopsies (2 cone biopsies and 21 incisional biopsies). The most clinically diagnosed lesions was cervical cancer (89 cases; 55.6%) followed by UV prolapse (30 cases; 18.8%) then symptomatic fibroid (8 cases; 5%), adenomyosis (6 cases 3.8%) while premalignant lesions and DUB had 2 cases each (1.25%). Those with cervical biopsies had clinical diagnosis of polyps and premalignant lesions [Table 1].

In benign tumor or tumor-like lesion, endometrial polyp was the commonest benign tumour followed by Nabothian cyst and squamous metaplasia which was 4 cases each (2.5%) and the least represented of benign tumor was two cases of Leiomyomatous polyp. In non-neoplastic lesions all the 20 cases seen were inflammatory with chronic non-specific cervicitis toping the lesion of which 12 cases (7.5%) occurred in UV-prolapse while plasma cell granuloma was one case with a frequency of 0.6% [Table 2].

The malignant cervical lesions were far more common & accounted for 55.6% of the entire cervical lesions, of which 83 cases (51.9%) were invasive Squamous Cell Carcinoma (SCC). The second commonest were adenocarcinomas with just 6 cases (3.75%). Among these invasive SCC, large cell non-keratinizing

Table 1: Showing type of surgical cervical specimen received within the study period

Type of surgery	Percent (%)
Hysterectomy	137 (85.6)
Incisional biopsy	21 (13.1)
Cone biopsy	2 (1.25)
Total	160 (100)

variants predominate with 39 cases (24.4%) followed by large cell keratinizing SCC with 34cases (21.3%) and then 6 cases (3.8%) of small cell non-keratinizing SCC, while clear cell SCC were just 3 cases (1.9%). Among the adenocarcinoma, malignant endometroid adenocarcinoma was the commonest with a frequency 1.9% followed by one case each for Malignant-Invasive papillary adenocarcinoma, Malignant-Mucinous adenocarcinoma of the cervix, and Malignant-Villoglandular adenocarcinoma [Figure1].

In premalignant lesions, High Grade Squamous Intraepithelial Lesions (HSIL) were commonest with 27 cases (79.4%) which included CIN2:15 cases (44.1%) and CIN3:12 cases (35.3%) making High Grade Squamous Intraepithelial Neoplasm (HSIL) far higher than Low Grade Intraepithelial Lesion (LSIL or CIN1) which were just 7 cases (20.6%) [Figure 2]. The ratio of HSIL to LSIL is 4:1 and the prevalence of these premalignant lesions in this research is 3.7%.

Table 2: Showing different lesions of cervical uterine.

Lesions	Frequencies	Percent (%)
CIN 1	7	4.4
CIN 2	15	9.4
CIN 3	12	7.5
Malignant SCC large cell non-keratinizing	39	24.4
Malignant SCC large cell keratinizing	34	21.3
Malignant SCC small cell variant	6	3.8
Malignant SCC clear cell variant	3	1.9
Malignant-microinvasive SCC	1	0.6
Malignant-endometroidadenoCA	3	1.9
Malignant-Invasive papillary adenocarcinoma	1	0.6
Malignant-Mucinous adenocarcinoma of the cervix	1	0.6
Malignant-Villoglandular adenocarcinoma	1	0.6
Chronic non-specific cervicitis	19	11.9
Endocervical polyp	7	4.4
Nabothian cyst	4	2.5
Squamous metaplasia	4	2.5
Leiomyomatous polyp	2	1.25
Plasma cell granuloma	1	0.6
Total	160	100

The mean age of cervical cancer as observed by this index study was 57.76 ± SD 12.63 which correspond with the mean ages of high grade squamous intraepithelial neoplasm; CIN3 & CIN2 having 59.92 ± SD 11.74 and 60.20 ± SD 11.21 respectively [Figure 3]. The mean ages of Malignant SCC Small cell variant are 59.83 ± 10.8, while that of Malignant SCC large cell non-keratinizing and large cell keratinizing are 58.44 ± 12.0 and 56.97 ± 13.9 respectively.

The peak age of all the malignant cervical tumor occurred in the 7th decade of life (61-70 age group) and accounted for 28 cases (31.4%) followed by 6th decade of life (51-60 age group) which accounted for 23 cases (25.8%) [Table 3].

Meanwhile the peak age of precancerous lesions occurred in the 5th and 6th decade of life and accounted for 10 cases each (29.4%). The LSIL (CIN1) occur more at younger age group of 40-50 years with a frequency of 57.1% (4 cases) while CIN

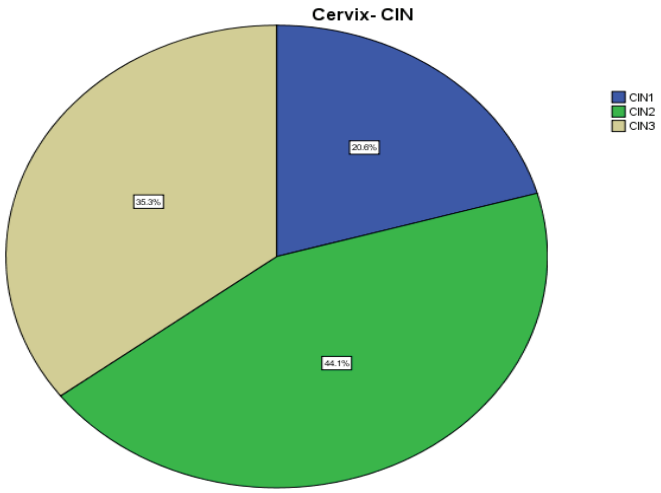

Figure 2: Showing precancerous lesions of the cervix with high grade squamous intraepithelial lesions predominating.

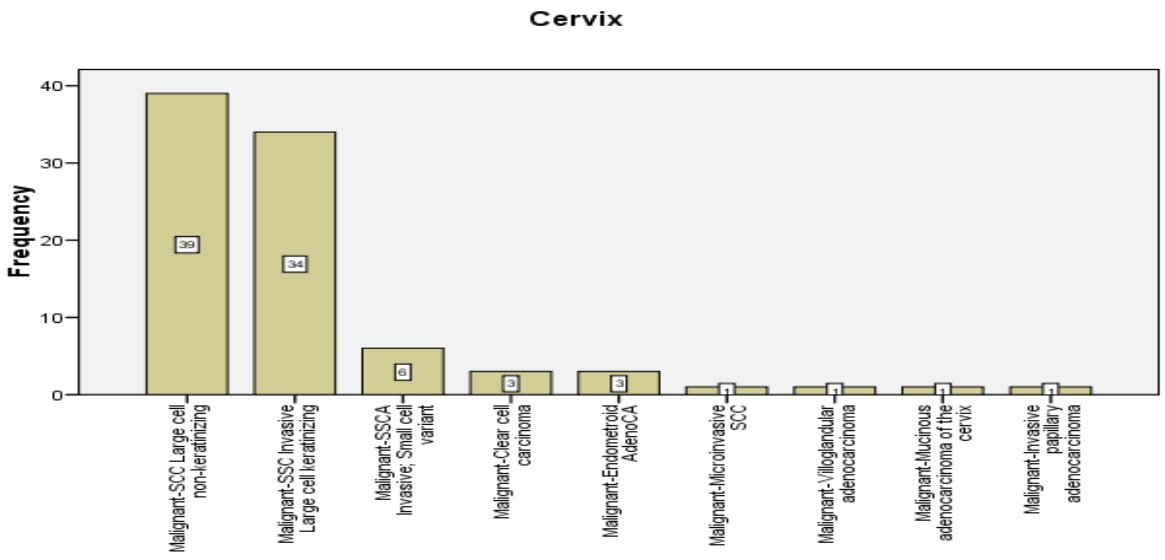

Figure 1: Showing different variants of malignant cervical neoplasm with SCC non-keratinizing predominating the tumours.

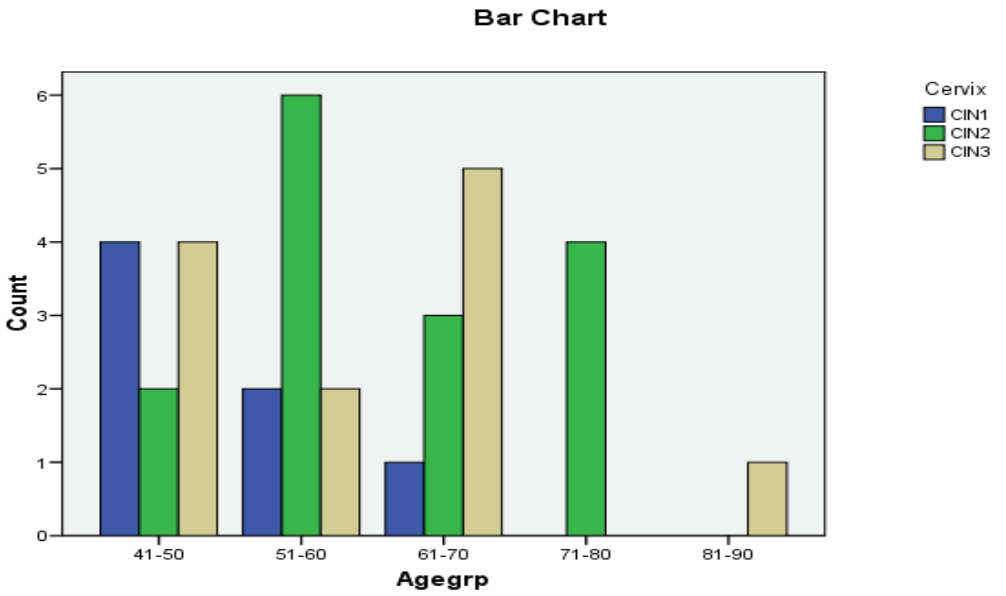

Figure 3: Bar-Chart showing the mean ages of cervical intraepithelial neoplasms.

Table 3: The age and frequency distribution of histological variants of malignant cervical tumours.

Age	SCC; large cell non-keratinizing	SCC; large cell keratinizing	SCC; small cell variant	SCC; clear cell variant	Microin-vasive SCC	EndometroidAd-enoCA	Papillary AdenoCA	Mucinous AdenoCA	VilloglandularAd-enoCA	Total (%)
0-10	-	-	-	-	-	-	-	-	-	0(0.0)
11-20	-	-	-	-	-	-	-	-	-	0 (0.0)
21-30	-	1	-	-	-	-	-	-	-	1(1.1)
31-40	2	4	-	1	-	-	-	1	-	8 (9.0)
41-50	6	8	2	-	-	-	1	-	-	17 (19.1)
51-60	16	5	1	1	-	-	-	-	-	23 (25.8)
61-70	9	12	2	-	1	3	-	-	1	28 (31.4)
71-80	4	4	1	1	-	-	-	-	-	10 (11.2)
81-90	2	0	0	-	-	-	-	-	-	2 (2.2)
Total (%)	39 (43.8)	34(38.2)	6 (6.7)	3 (3.4)	1 (1.1)	3 (3.4)	1 (1.1)	1 (1.1)	1(1.1)	89(100)

Table 4: The age and frequency distribution of premalignant cervical lesions.

Age group	CIN1 (LSIL)	CIN2 (HSIL)	C1N3 (HSIL)	Total (%)
41-50	4(57.1)	2 (13.3)	4 (33.3)	10 (29.4)
51-60	2(28.6)	6 (40.0)	2 (16.7)	10 (29.4)
61-70	1 (14.3)	3 (20.0)	5 (41.7)	9 (26.5)
71-80	-	4 (26.7)	-	4 (11.8)
81-90	-	-	1 (8.3)	1 (2.9)
Total (%)	7 (100)	15 (100)	12 (100)	34 (100)

Table 5: Types of cervical lesions (according to World Health Organization (W.H.O) classification).

Types	Pre-malignant (%)	Malignant (%)	Benign (%)	Total (%)
Epithelial tumours SCC and precursors	HSIL, LSIL (n=34;24.3%)	SCC: (N=83;59.3%)	Squamous metaplasia (N=4; 2.8%)	121 (86.4%)
Glandular tumours and precursors	-	ADENOCA (n=6;4.29%)	-	6 (4.29%)
Benign glandular tumour and tumour-like lesions		-	Nabothian cyst (4) and endocervical polyp (7) (n=11;5.44%)	11 (7.86%)
Other epithelial tumours	-	-	-	0
Mesenchymaltumour & tumour-like lesions		-	Leiomyomatous polyp (n=2; 1.36%)	2 (1.43%)
Mixed epithelial &mesenchymaltumours	-	-	-	0
Melanocystictumours	-	-	-	0
Germ cell tumour	-	-	-	0
Lymphoid & myeloid tumours	-	-	-	0
Secondary tumours	-	-	-	0
Total (%)	34 (23.2%)	89 (60.5%)	17 (16.3%)	140 (100%)

2 and CIN3 occurred more at higher age groups of 51-60 and 61-70 years with frequencies of 40.0% and 41.7% respectively [Table 4 and Table 5].

Discussion

The majority of specimens in the histopathology department were gynecological cases. Over the five-year study period, NAUTH department of pathology received 160 uterine cervical specimens. The uterine cervix is prone to develop several nonneoplastic and neoplastic lesions.

In this study, the frequencies of malignant, benign and premalignant lesions were 55.6%, 23.1% and 21.3% respectively with cervical malignancies being the commonest lesion. The second common cases were benign lesions of which inflammatory non-neoplastic lesion predominantly non-specific cervicitis were the commonest. These findings were in contrast with most literatures where inflammatory lesions formed the major part followed by cervical malignancies. The reasons for this may be attributed to the types of specimen, clinical diagnosis for the surgery and ease accessibilities to antibiotic use. In NAUTH histopathology department, majority of our specimens were hysterectomies with few cervical biopsies and most of these specimens were majorly based on clinical diagnosis of cervical cancer (89cases), UV-Prolapse (30 cases), symptomatic leiomyoma (8 cases), adenomyosis (6 cases), premalignant lesions (2 cases), DUB (2 cases)and not inflammatory lesions. Moreover, most of the inflammatory lesions in our centre are diagnosedcytologically and treated accordingly with subsequent repeat of the pap-smear to ascertain adequate treatment. Only those with cytologic abnormalities would proceeds to biopsy or hysterectomy. In addition, cervical cancer in Africa is still a great burden and its prevalence cannot be over emphasized in most under-developed countries in which Nigeria belongs. It is the second most common cancer after breast cancer and the commonest female genital tract malignancy in the third world nation. [2] In Africa, cervical cancer accounts for 22.2% of all cancers in women and it is also the most common cause of cancer-related death among women in Eastern, Western and Middle Africa; Central America; South-Central Asia and Melanesia.[9]Indiscriminate and ease accessibilities to use of antibiotic may be a factor.

Although, most literatures concur that majority of the specimen received were hysterectomy; however, their clinical diagnosis were majorly samples not suspicious of malignancies. Nidhi Gupta et al., Poste P et al. and Srivani et al., received hysterectomy (81.81%) as the most common specimen in their studies similar to index study of 85.6%. [10,11]

Furthermore, Reddy et al. and Gupta et al. reported higher percentage of non-neoplastic lesions with 78.4% and 80.9% respectively. [10,12] Nwachokor et al. reported relatively higher percentage of malignant lesions 43.7% compared with most literatures with 56.3% of benign lesions. [13]

In Nwachokor et al. study, inflammatory lesions and tumour like lesions accounted for 59.8% and 40.2% of non-neoplastic cervical lesions respectively. [13] This is in tandem with index research, where the inflammatory lesions and tumour like lesions among the benign cases were 54.1% and 45.9% respectively. Moreover, almost all the inflammatory lesions observed in index research were chronic non-specific cervicitis similar to reports done by Omoniyi-Esan et al., Pandit et al., Gupta et al. and Reddy et al. [1,10,14] The most common invasive carcinoma in this study was Squamous Cell Carcinoma (SCC) with 93.1% followed by adenocarcinoma (6 cases; 6.8%), with SCC large cell non-keratinizing variant being the commonest 44.3% (39 cases) followed by SCC large cell keratinizing subtype 34 cases (38.6%). The least common was small cell non-keratinizing subtype 6 (6.8%). This is similar with most work done by researcher such as Mandakini et al., Reddy et al., Gupta et al., and Mandakini et al. reported 67 cases of SCC out of 72 cases (93.05%) and 5 cases of adenocarcinoma (6.95%). [15] Reddy et al reported 92.72% of squamous-cell carcinoma and 6 cases of adenocarcinoma (3.64%), with 97 cases (61.70%) of SCC large cell non-keratinizing subtype, followed by large cell keratinizing type in 30.50% (48 cases) while the least common was small cell non-keratinizing type. [12] Gupta et al. also reported 13 cases (86.6%) of squamous cell carcinoma out of all 15 malignancies followed by 1 each case of Adenocarcinoma (6.7%) and HSIL (6.7%) while Srikanth, reported 84% cases of Squamous cell carcinomas followed by 1 each case of Adenocarcinoma (6.7%). [10,16]

Premalignant cases were the third most common cervical lesion in this present study with a prevalence of 3.7% and a frequency of 23.2% (34 cases) having 27 cases (16.9%) of HSIL and 7 cases (4.4%) of LSIL amounting to a ratio of 4:1. The prevalence of precancerous lesion in this study is in tandem with previous (1992) and recent (2019) reports from Cameroon with 3.9% and 3.33% respectively. [17] Current study in Nigeria and Côte d'Ivoire as well as in Botswana, also show lower prevalence with 6%, 11%and 15.2%, respectively.[18,19]In contrary to higher prevalence rate found in Central African Republic Africa (16.4%), South Africa (66.3%), Uganda (73%), Zambia (76%) Kenya (26.7%) and Rwanda (24.3%). [20] In developed countries such as France, the prevalence of precancerous cervical lesion rate is much lower at around of 0.5%. The difference of prevalence of the precancerous lesions of the uterine cervix from one country to another is mainly due to differences in the sexual practices, the existence and consistency of screening programs and management options implemented in these countries. [17] Again, in this research with a low prevalence rate of 3.7% the reason may also be attributed that Nnewi being in the South-eastern part of Nigeria where strong cultural and religious support on marriage as well as less lifetime sexual partners may contribute.

In this study the peak age of the entire malignant cervical tumor occurred from 51-70 age groups while the peak age of precancerous lesions occurred from 41-60 years. The only one micro invasive cervical carcinoma we had occurred at 68 years. The LSIL (CIN1) occur more at age group of 40-50 years while CIN2 and CIN3 occurred more at age groups of 51-60 and 61-70 years respectively. The index research is somewhat similar with report done by Juan et al. who reported that an average age of patients with invasive squamous cell carcinoma is 51.4 years 15 to 23 years older than patients with CIN 3, and 8 years older than patients with micro invasive carcinoma and that it can

also occur in any age between 17 and 90 years. Juan et al. also reported that LSIL occur in early reproductive years (ages 16 to 26) or at the onset of sexual activity but it may also become somewhat more common in mid to late menopause (older than 58 years) while HSIL are most prevalent in women in their mid to late reproductive years (ages 26 to 48), although they may be seen at any age after the onset of sexual activity. [2]

The commonest benign tumour of the cervix seen in this study is endocervical polyp which is in tandem with most literatures. Moreover, we saw only 2 cases of cervical Leiomyomatous polyp indicating the rarity of this benign tumour in the cervix.

Conclusion

Since invasive cervical lesions far exceed benign cervical cases in our environment, it is invariable that majority of HSIL lesions progress to frank malignancy and therefore cervical screening is of paramount importance. In addition, SCC was commonest carcinoma with large cell non-keratinizing histologic subtype predominating. Endocervical polyp is the commonest benign tumor of the cervix while cervical Leiomyomatous polyp is very rare.

Competing Interests

The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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