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The Occurrence of Uterine Benign Diseases and their Histomorphologic Characters

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Abstract

Uterine diseases are several and can develop from any part of the organ. Noticeable benign diseases are type called hydatidiform mole considered benign among gestational trophoblastic disease and is said to occur from abnormal fertilization of abnormal ova. Other forms are inflammatory, proliferative of insidious cell/tissue implant, hormonal induced, and infectious in their origin. Samples were obtained from patients consulted and admitted into Department of Morbid Anatomy of Ebonyi State University Teaching Hospital. Clinical and histopathological record books were reviewed alongside processed tissues, and slides stained by popular heamatoxylin and eosin technique in the 3 year study period. Of the 642 gynecological samples searched, result showed a progressive increase in number as the years empty from 2011 to 2013 presenting 8 uterine diseases in a population of 116 cases. A total of 518 cases were product of conception of which 250 were as a result of incomplete spontaneous abortions and 200 inappropriate criminal abortions, while 68 could not be associated with any definite cause. Leiomyoma cases were 75%, uterine/vaginal prolapsed were 6%, molar pregnancies and endometriosis 5% and while endometrial hyperplasia and uterine atrophy were 3% each and 2% each were for uterine polyp and adenomyosis in all of the 116 cases. Six age groups were involved showing that 7 diseases and total frequency of 50% occurred with age group (40-49) and is seconded by (30-39) which had 5 conditions with frequency of 21%. Attempted provisional diagnosis was based on clinical presentations, and of 116 cases 80% were confirmed accurate by laboratory diagnosis. Clinical characters of leiomyomas were the same while histomorphologic features were not entirely consistently same in all.

Keywords: Uterine benign diseases; Histomorphology; Occurrence; Age group; Clinical features

Introduction

Various diseases affect the uterus and they are broadly grouped into Inflammatory, Benign and Malignant diseases [1]. Majority of benign lesions of this organ have inflammatory origin suspected to have been caused by infection from microorganisms, while the periodic influence of female hormones on the composite tissue is accused of promoting sudden insidious and genetic diseases in the population [2]. Some of the benign diseases of the uterus have high incidence rates, most common being leiomyoma and is considered to be the most common pelvic tumors and the most common noncancerous tumors in women of child bearing age [3]. It is said to be prevalent in women over the age of 30 years in which as many as 1 in 5 may have fibroid during their childbearing years [4].

Most fibroids are asymptomatic, producing clinical emergency of heavy and painful menstruation, painful and post-coital bleeding, and urinary frequency and urgency, infection and delayed pregnancy [5,6]. It has been documented that 20 to 30% of women above the age of 30 years harbour uterine fibroids, which account for 3.2-7.6% of new gynecological cases and 68.1% of hysterectomies [7].

Leiomyoma develops from smooth muscle tissue layer of the uterus [8] and can transform to malignancy [9]. Uterine hyperplasia is found to involve two basic tissue types the endometrial and myometrial. The commonest type is endometrial hyperplasia, while adenomyosis is considered when endometrial gland proliferation and its implantations occur in the myometrium.

Most cases of endometrial hyperplasia result from high levels of estrogens combined with insufficient levels of the progesterone-like hormones. The conditions may occur in wide range of settings such as in obesity, polycystic ovarian syndrome, estrogenic dependent tumors (e.g. granulos cell tumor) and in certain estrogenic replacement therapy [10].

Endometriosis is another common form of benign diseases of the uterus with incidence rate of about 6-10% worldwide and is present in 35-50% of child bearing women. The lesion/occurrence is oestrogen-dependent and capable to persist beyond menopause with resultant hysterectomy in up to 40% of patients [11].

Endometriosis is a condition associated with the implantation and proliferation of endometrial cells elsewhere other than the cavity of the uterus as commonly observed on the membrane lining the abdominal and peritoneal cavities of a female. Though several symptoms that characterize lesion may depend on the site of active endometriosis, various reports have shown that pelvic pain is common and do consequent significant social and psychological impact [12].

Gestational trophoblastic disease (GTD) occurs rarely and types are based on the broad spectrum of cellular proliferations arising from the

placental villous trophoblast. Five differentiated clinicopathologic forms have been identified and they include hydatidiform mole i.e. (complete and partial) and invasive mole, while choriocarcinoma, epithelioid trophoblastic tumor and placental site trophoblastic tumor exist as well. However, the term "gestational trophoblastic neoplasia" (GTN) have consistently been used for four of the conditions found with capability to progress, invade, metastasize, and lead to death if left untreated [13].

According to inflammatory diseases of the uterus are majorly caused by infections and classic example is the Pelvic inflammatory disease which can spread from the uterus to fallopian tubes and/or ovaries and progresses to scar formation with adhesion nearby tissues and organs [14]. Though histopathologic characters showcase acute or chronic inflammatory cells, the individual cell kind involvement offers site identification and characterization of lesion.

Hence endometritis may be acute or/and chronic inflammation of the inner lining of the uterus caused by microorganism infection [15]. Symptoms include lower abdominal pain, fever and abnormal vaginal bleeding or discharge.

Diagnosis of uterine diseases begins with clinical manifestation suggestive of such diseases. Laparoscopy, endoscopy, X-rays and ultrasound are usually more often used in the diagnosis of most uterine growths. Histopathologic examination of uterine tissues is usually for confirmation, identification, characterization and prognosis of clinical and other diagnoses made, in which a study revealed that 1.6% diagnosed of adenomyosis and various uterine hyperplasias were able to transform to endometrial cancer [16].

The 3 years search of benign uterine diseases occurrence within eastern Nigeria was to ascertain the age distribution, frequency, prevailing pattern, and histomorphologic characters that march these lesions and ascertain whether such features possess the capability to transform with possible identifiable trails into malignancy. The study is to unearth the possible risk factors of these diseases in a developing healthcare delivery system.

Methods and Material

The retrospective study spanned over a period of three years (2011-2013), involving 642 female patients whose clinical folders, laboratory request forms and results were traced to Department of Morbid Anatomy and record books were consulted at Department of Obstetrics and Gynecology unit, Federal Teaching Hospital Abakaliki formerly Ebony State University Teaching Hospital, Abakaliki.

The Hospital is located at northeast of Igbo land with population majorly characterized by peasant farmers, handful of traders and civil servants. Clinical records and histopathology report books were reviewed alongside processed tissue blocks and slides in the three year study. The remaining gross or fragments samples of which tissue blocks and slides were made from were searched to ascertain and authenticate the origin of tissue blocks and slides.

Tissue blocks and corresponding slides were sought and reviewed microscopically alongside all corresponding histopathology reports. Also clinical history of patients assessed were used to considered accuracy of request for laboratory testing of samples and results.

All clinical records irrespective of sufficient patient history must be satisfactory and met the criteria for inclusion if tissue blocks and slides are traced to it. New slides were made from these blocks, stained by popular Harris's heamatoxylin and eosin staining technique, and diagnosis in comparison with histopathology reports is confirmed.

Results

A total of 642 gynecological samples were received at the Federal Teaching Hospital Abakaliki, Ebonyi State of which 114 were in 2011, 213 in 2012 and in 2013 a progressive total of 315. Of these 518 cases were products of conception reviewing 250 cases of incomplete spontaneous abortion, 200 criminal abortions and 68 cases of undetermined associated causes; 116 cases were benign lesions distributed among several uterine lesions, 3 were malignant, and 5 were normal uterine tissue.

Of the 116 cases, 8 benign diseases were found incriminating including 87 (75%) leiomyoma, 7 (6%) uterine/vaginal prolapse, 6 (5%) each for molar pregnancies and endomethritis, 3 (3%) each for endometrial hyperplasia and atrophy, and 2 (2%) each for uterine polyp and adenomyosis. The patients involved had their ages grouped into 6 and diseases distribution and frequencies among the groups were as in Table I.

Age group	20-29	30-39	40-49	50-59	60-69	Total
Leiomyoma	18	51	16	2	-	87
Molar Pregnancy	2	2	2	-	-	6
Uterovaginal Prolapsed	-	-	1	2	4	7
Uterine Polyp	-	1	1	-	-	2
Endometrisis	-	3	2	1	-	6
Endometial Hyperplasia	-	-	1	2	-	3
Endometial Atrophy	-	-	1	2	3	3
Adenomyosis	-	1	1	-	-	2
Total	20	58	24	8	7	116

Table 1: Various benign uterine diseases the distributions and frequencies among age groups.

Age group (30-39) experienced the second highest occurrence of benign uterine diseases of 5 conditions which altogether gave highest total frequency of 58 (50%), while age group (40-49) has highest occurrence of 7 conditions and is second highest in total frequency of 24 (21%).

Of the 8 diseases that occurred, provisional diagnoses attempted were based on clinical presentations by all patients, such that the degree of accuracy per condition conflicts because more than one disease presents the same clinical characters though few variations exist. Of the 116 patients, 93 (80%) of provisional diagnoses were confirmed accurate by histomorphologic features, 23 (20%) were unconfirmed and wrong. Also clinical features of leiomyoma was searched and found as in Table 2 and histomorphologic features were not consistently the same for all and leomyoma showed several (Figures 1A-1C).

Symptoms	Frequency	Percentage
Menorrhagia	27	31%
Lower abdominal mass	21	24%
Abdominopelvic pains and discomfort	10	12%
Infertility	9	10%
Dysmenorrhea	7	8%
Irregular vaginal bleeding	6	7%
Urinary frequency/urgency	4	5%
Recurrent abortion	3	3%

Table 2: Clinical characters of leiomyoma as observed on patients.

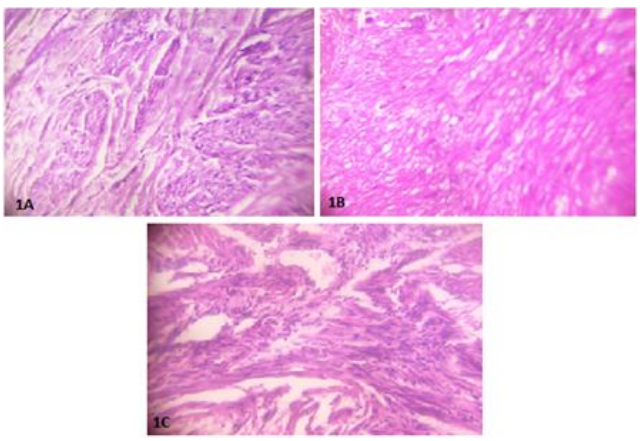

Figure 1A: Whorl appearance of leiomyoma H & E stained X40. B: Typical cystic and fatty cell reaction cells within the fibrous elements in Leiomayoma. H & E Stained X40. C: Edematous myometrium invaded by mononuclear cell; nuclear features are typical and benign, H & E Stained X40.

Discussion

The prevalence of uterine diseases in different parts of the world especially among the Caucasians is a well-studied subject. However, such epidemiological data is unavailable in Ebonyi State especially since the merging of the former Ebonyi State University Teaching Hospital (EBSUTH) and the Federal medical Center (FMC) Abakaliki. This present study is therefore aimed at providing data of the incidence of some of the benign uterine diseases including leiomyoma, molar pregnancies, uterine prolapse, endometrial atrophy, endometrial hyperplasia, uterine polyp etc.

The collection of samples for any histopathological study is dependent on the clinical indications, and most times sampling is always guided by the fact that numerous investigations can be requested of one specimen/sample type. Clinical indications for uterine sampling are for investigation of abnormal uterine blood, the evaluation of the involvement of the endometrium with cases of infertility and for endometrial hormonal assessment.

Consequently, the indications which are hormonal influenced may determine the appropriate sampling method and time. This may be dilation and curettage (D&C) or biopsectomy. It is also true that curettage is carried out as excision biopsy of the endometrium but area of sampling should be well recognized and noted [17]. The demerits of this technique is mechanical distortion of lesions such as record for leiomyomas and polyps, perforation or resultant amenorrhea associated with Asherman's syndrome which can wrongly influence the patterns and morphologic architecture of lesions and normal biopsy [18,19]. The popular endometrial biopsy (EMB) done in the office without anesthesia have been improved upon with new technology but is only to reduce patient discomfort during procedure and not for improved quality of sample [20-23]. The same was the case observed in our study. Does it mean that several challenges agued upon in favor of sampling techniques for patients' safety by many investigators are the only comfort zone reason for uterine sampling?

The same reason was observed in this study as the heart burner for uterine specimen collection without regards against diagnostic artifacts; hence wrong diagnosis. Also it was discovered that certain sampling technique suffices better for uterine hyperplasia and carcinoma particularly with the inclusion of hysteroscopy and ultrasound as supplementary diagnostic techniques when clinical indication is abnormal bleeding as in other studies [24-30].

These were found as some of the methods employed for sampling in this study. Still arguable is that sample/specimen distortion was not in any time considered during and after sampling save for specimen fixation in 10% formal saline. Has this neglect in appropriate sampling produced distorted sample/specimen? In attempt to adduce answer, simple light microscopy without special staining techniques is inadequate.

In the current study, uterine fibroid was found to be the most frequent uterine disease in the study population, with a frequency of 30.1% of all gynecological samples received at the Federal Teaching Hospital Abakaliki. This incidence rate is similar to that reported in Massachusetts, USA, in which they reported an incidence rate of 8.9% among the whites and 30.6 among the black women [31]. The prevalence in Aminu Kano Teaching Hospital Kano as reported by Abiodun O and Belga F was 24.7% [32]. In the study which covered the period between 2003 and 2007, they observed that uterine fibroids had a period prevalence of 24.7% of all major gynecological operations in Aminu Kano Teaching Hospital Kano.

In Nnewi, Nigeria, uterine leiomyoma constituted 117 of the 1094 gynecological admissions during the study period (10.7%) of 4 years (between 2002 and 2006) [33].

It was observed in the study that, the most common benign uterine disease was leiomyoma having a prevalence of 70% of all benign uterine diseases studied. This incidence rate agrees with the world wide prevalence of uterine fibroid. In America, it is estimated that Eighty percent of African American women will develop benign uterine fibroid tumors by their late 40s, according to the National Institute of Environmental Health Sciences [34].

Subjects within the age range of 30-40 years had the highest frequency of uterine fibroid. The frequency was 58.1%. In Nnewi Nigeria, it was observed that the majority of the patients with leiomyoma were between the ages of 30-44 years (a frequency of 75.6%) [33]. In America, it was equally reported that uterine fibroid among the black American women was more prevalent in the younger and middle aged women (between the ages of 25-40) [35].

The major clinical presentation seen in patients was menorrhagia (bleeding per vagina) followed by lower abdominal mass, although most of the patients presented with more than one symptom. This indicates that most of the complaints by the patients were either bleeding per vagina or presence of lower abdominal mass. This was equally reported in the study in the South-west region of Nigeria where about 47.7% of clinical symptoms of fibroid was lower abdominal mass, followed by menorrhagia with a frequency of 39.1% [36]. Other clinical presentations observed in the study area were, infertility, urinary incontinence, abdominal discomfort and dysmenorrhea.

Other benign uterine diseases observed in the study population were molar pregnancies, uterovaginal prolapse, uterine polyp, endometrial atrophy, endometrial hyperplasia and adenomyosis. The incidences of these other benign diseases were between 1.6 to 4.8% of all benign diseases in the Federal Teaching Hospital Abakaliki. These constituted less than 1% of all gynecological complaints. Although most of these diseases may present with similar symptoms like menorrhagia, dysmenorrhea, abdominal comfort as documented elsewhere. In this study area, majority of patients that present with these symptoms are almost always diagnosed to have uterine fibroids. Several morphologic patterns were observed for leiomyoma with varied components apart from the whorled trabecular appearance as in Figures 1a-1c and myometrial cell nuclear disposition also differs awhile particularly among oedematous stroma [37,38]. Fatty cell implantation in the myomerium observed has been reported though nuclear characters were not described [39].

Two types of nuclear pleomorphism were found of Fat cells i.e. oval and oblong suspected to have resulted from varying degrees of cytoplasmic fat accumulation (Figure 1b). Mitotic activity apparent but at minimal degree and absent with less fat filled cytoplasm is noted. A characteristic lace-wool morphologic pattern (clear cells) is prominent at some areas while at other area where fat cells with enlarged cytoplasm are found they are also crowded by other fat cells of varied sizes.

This pleomorphism in nuclear features and cytoplasm are capable of inducing focal fat cell death resulting to awful transformation observable under light microscope. These findings have not been reported to our knowledge to belong or describe the so called lipoleiomyoma.

Another pattern not often found in combination is as in Figure 1c, which show poorly formed glands planted in the myometrium. The glands have their lumen partly filled with homogenous eosinophilic staining material which may be absent in others. The cells lining mostly atrophic less tortoise walls have nuclear mitotic figure increase which cannot be easily graded because of the staining technique employed. This finding is discretely distributed in the slides and at other areas revealed three types of nuclear features i.e. oval, elongated but thickened at any point along the nuclear length, and irregular without obvious evidence of nuclear material mitosis. This pattern has been reported previously in other studies, particularly with reactive myometrial stroma cells exhibiting nuclear pleomorphism without oedema and mononuclear inflammatory cells [40].

The uterine hydatidiform mole was observed in 6 of all uterine samples during the year of study as previously published [41]. All were 5 complete moles typically featuring avascular and vascular hydropic chorionic villi and 1 was partial mole with hydropic chorionic and normal villi accompanying some atypical cytotrophoblastic cells (Figure 2).

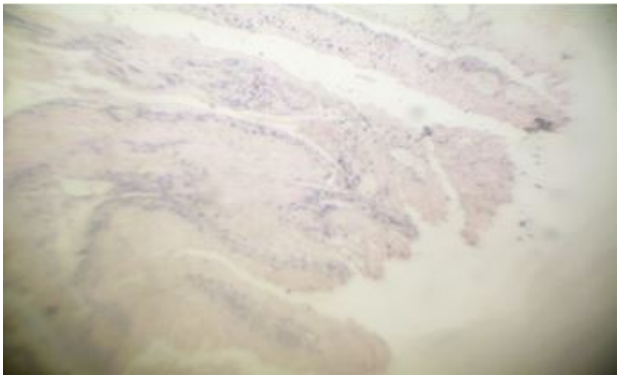

Figure 2: Complete mole, showing edematous villi and infiltrating inflammatory cells, H & E Stained X40.

Focal areas of mixed inflammatory cell infiltrates were apparent in all types, and mononuclear cells were present in all cases and infiltrated most in and within the cytotrophoblastic and syncytiotrophoblastic walls while minimal numbers were discretely distributed particularly among obvious trophoblasts. Finding lacked areas of necrosis rather oedema was obvious as in a study [42].

If inflammatory process engenders or promotes cell transformation to awful side of malignancy, time therefore is the prime factor for mole pregnancy to transform as inflammatory cell action continues in the presence or absence of other factors with embryonic cell as these, though studies have shown genetic abnormality of types [43,44]. After all, necrosis is one of the inherent outcomes of inflammation. From the clinical record books, all patients in the study had vaginal bleeding within 3 weeks prior to evacuation, lower abdominal pains, and recurrent incidence was observed in one case of complete mole. Dough consistency and slight tender uterus at 21 weeks of suspected pregnancy was observed with the only partial mole case. These clinical findings and others are strong indications for evacuation against delay that cause eventual transformation into intermediate trophoblastic tumors and tumor-like lesions [45].

All six (6) cases of endometritis in this study were chronic rather than only specific granulomatous endometritis as in Figure 3 [46,47]. Few sheets of xanthoma cells are present with reactive stroma of fibrous features and failed attempts of glands formation as in two of the cases. In serial slide sections were observed heavy mixed inflammatory cells preponderant of which are mononuclear cell and

poorly formed lymphoid follicles [48,49]. Though that these types of findings have been reported before but scanty stroma element was not mentioned as is obvious in this study.

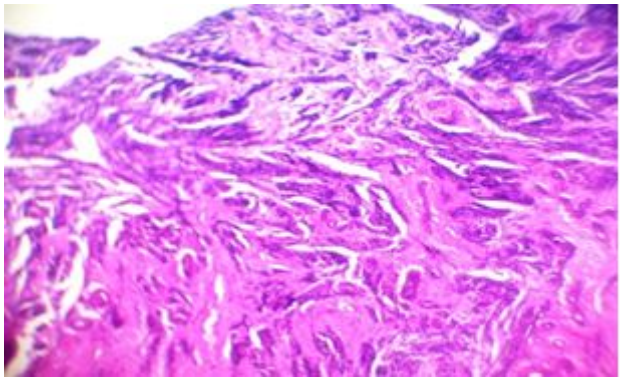

Figure 3: Endometritis; inflammation and loss of the uterine endometrium to the erosion of myometrium by mixed leucocyte infiltrate from complicated PID; H & E Stained X40.

Chronic endometritis has been said to occur in postpartum endometrium and is considered normal even with associated menstrual abnormalities and pelvic pains though late clinical indicators were the major reasons for sampling in this study. The age relationship to the lesion in this study is between 30 to 50 years, and varied in agreement with that informed for xanthomatous endometritis of being most frequent in elderly and that it is associated with cervical stenosis and pyometra was not confirmed as the former lesion occurred sparingly in the search [50,51].

The situation is not the same with product of conception (POC) in which two clear pictures are apparent. In the first, almost all the slides are truly represented in Figure 4 of this study and are acellular with unstained clear microscopic fields and globes of fat.

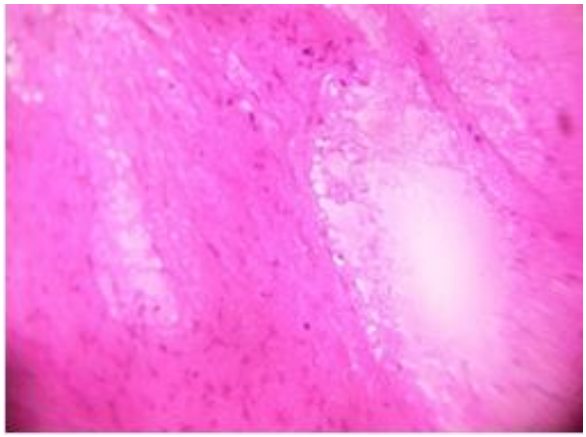

Figure 4: Typical Histomorphological feature of Product of Conception (POC). H & E stained, X40.

Few areas of cell component revealed decaying features that is not worthy for inclusion. This is not the same with the second in Figure 5, which showed highly cellular content with nuclear pleomorphism though edematous entity was present before fixation.

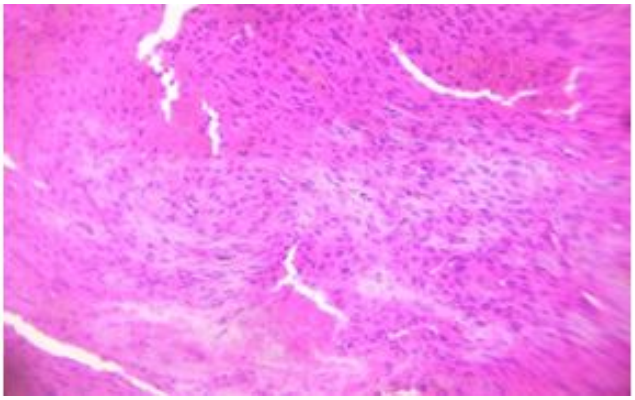

Figure 5: Edematous morphological features in POC, H & E stained X40 obj.

Uterovaginal prolapsed occurred in 7 patients of age mostly 50-69 to be second most frequent observed lesion in the study (Figure 6). The age consequence is associated with parity, post-surgical complication of infection and genetic makeup of patients as is in some studies and these were finding in two patients in this study [52,53].

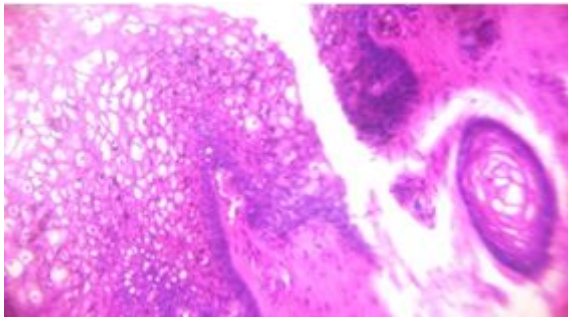

Figure 6: Hyperplastic growth from prolapse of the uterovagina. H & E Stain. X40.

Clinical indications ranges from bleeding per vagina, irregular post-menopausal bleeding, pains and repeated microorganism infections and these moderated technique of sampling to curb bleeding as well as diagnosis had been common practice. Histomorphologic pattern denotes inflammatory response by the active infiltration mononuclear cells, erosion, hyperplasia and frantic metaplasia at uterovulva junction. Nuclear staining of mostly cuboidal squamous cell lining junction is basophilic and mitotic activity is present. Are not all these features and patterns of borderline benign lesion criteria considered for easy vulva cell transformation to cancer as reported in previous studies [54,55]. From this study it is important to insist that cellular transformation as investigated is possible, probably undiscovered factor prevented it.

Conclusion

This study compares favorably with others in our environment and has not shown any huge difference with respect to incidence, clinical presentation and complications of myomata. In conclusion, the incidence rate of benign uterine diseases in Federal Teaching Hospital Abakaliki shows that leiomyoma has a high prevalence rate in Abakaliki, Ebonyi State as in other areas in Eastern Nigeria. The other benign uterine diseases however had a relatively low prevalence when compared with other studies. There were evidence from this study that other benign lesions of the uterine corpus may appear less frequent in occurrence but possesses nuclear potential and patterns favorable for transformation into cancer.

Also the uterine fibroid was more in the patients aged between 30 to 40 years and morphologically may contain component and pattern which sometimes in the presence of heavy inflammatory cell infiltration show nuclear pleomorphism of cellular content. Moreover, the commonest symptoms presented by the patients were menorrhagia and lower abdominal mass.

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