MORPHOLOGICAL PATTERN OF ENDOMETRIAL BIOPSIES IN SOUTH-WESTERN NIGERIA

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ABSTRACT

Background: Endometrium remains the most sensitive indicator of ovarian function and endometrial biopsy is one of the diagnostic procedures in endometrial pathology. The current study was carried out to examine the morphological pattern of endometrial biopsies in Ibadan, South-western Nigeria and compare the results with similar studies.

Method: A retrospective study was undertaken to review all cases of endometrial biopsies received in the Department of Pathology, University College Hospital, Ibadan between January 1999 and December 2008. The patients' data were retrieved from the surgical pathology daybooks and Histology Request forms. The neoplastic lesions were classified according to 2003 World Health Organization classification for endometrial neoplasms.

Results: A total of 2,444 cases of endometrial biopsies were received during the 10-year study period. The functional endometrial changes were the most common histopathological diagnostic category, accounting for 53.8% (1035) of cases. Other pathological diagnoses included endometritis (7.8%), simple endometrial hyperplasia (5.8%), partial hydatidiform mole (2.3%), complete hydatidiform mole (2.1%) and malignant neoplastic lesions (3.9%). Infertility was the most common (57%) indication for endometrial biopsies followed by uterine bleeding (33%) while the least common clinical indication were the menstrual disorders (10%).

Conclusion: The functional endometrial changes account for the highest morphological patterns while malignant lesions account for the least pattern of the endometrial biopsies evaluated for etiological basis of infertility, uterine bleeding and menstrual disorders in Ibadan. Infertility was the commonest indication for endometrial biopsies while the least common clinical indication was menstrual disorders.

Keywords: Endometrium, Biopsies, Morphology, Ibadan

INTRODUCTION

Endometrial biopsies are among the most common specimens submitted for histopathological analysis.[1] Endometrial biopsy is a safe, efficient and cost-effective means of evaluating the uterine endometrium. The procedure is usually associated with minimal discomfort and is easily accomplished in the outpatient setting. In the United States of America (USA), endometrial biopsy is used most often in the perimenopausal or postmenopausal woman to evaluate abnormal uterine bleeding and to rule out endometrial cancer[2, 3] while in Nigeria, it is used most often in the evaluation of infertility.[4,5,6] It also serves to identify other hormonally induced changes in the uterine lining. In general, the biopsy assists in the identification of causes of abnormal uterine bleeding, evaluate dysfunctional uterine bleeding, rule out endometrial carcinoma and precancerous lesions,

identify causes of postmenopausal bleeding, evaluate infertility (specifically short luteal phase) and follow up presence of endometrial cells on Pap smear. It is virtually indispensable for the diagnosis of genital tract infections including tuberculosis and as a means of culturing the mycobacterium for antibiotic sensitivity testing so that appropriate therapy can be given.[2,3]

Endometrial biopsy is sufficiently sensitive to allow accurate diagnosis of endometrial hyperplasia and or carcinomas. However, endometrial biopsy may fail to detect other uterine pathologies such as polyps and submucous leiomyomas.[2,3]

Few Nigerian studies have examined the morphological patterns of endometrial biopsies at different times, in different places. These include studies by Ekanem *et*

al.[4] in 2006, from Calabar, South-South Nigeria, Dauda *et al.*[5] in 2005, from Jos, North-central Nigeria, Ikeme *et al.*[6] in 2004, from Enugu, South-eastern Nigeria, Idrisa *et al.*[7] in 2000, from Maiduguri, North-eastern Nigeria, Iyare [8] in 2005, from Lagos, South-western Nigeria, Ojo *et al.*[9] in 1990, from Ilorin North-central, Nigeria, and Adewole *et al.*[10] in 1989, from Ibadan Nigeria. Most of these studies reported low prevalence of endometrial hyperplasia and endometrial cancer. Howbeit, there still exists a paucity of studies on the general morphological pattern of endometrial biopsies in the Nigerian literature.

This study was therefore undertaken to analyse the morphological pattern of endometrial biopsies in women who presented with infertility, uterine bleeding and menstrual disorders at the hospital.

MATERIALS AND METHODS
A retrospective study was undertaken to review the histopathological reports of all endometrial biopsies at the Department of Pathology, University College Hospital, Ibadan from January 1999 to December 2008. Patients' data were extracted from the surgical daybooks, case notes, Histology Request forms and from the Cancer Registry.

Individual cases were verified by retrieving and histologically examining the original glass slides. The paraffin blocks of cases in which the original slides could not be retrieved were re-cut and stained with haematoxylin and eosin. Histochemical stains to demonstrate acid-fast bacilli (Ziehl-Neelsen stain) or fungal organisms (Gomori methenamine silver and periodic acid-Schiff stains) were carried out on cases of chronic granulomatous inflammation for possible identification of the causative agent. Excluded from this study were products of conception for therapeutic purposes, cases where both slides and blocks could not be found or inadequate clinical details and endometrial specimens obtained other than by curettage or biopsy, e.g. hysterectomy specimens. The neoplastic lesions were classified using the 2003 World Health Organization Classification for endometrial neoplasms.[11] The data obtained were analysed in terms of frequency and age distribution using the Statistical Package for Social Sciences, version 20. The data were presented in proportion, frequency tables and figures.

Ethical clearance for the study was obtained from the Joint University of Ibadan/University College Hospital Ethical Review Committee .

RESULTS
A total of 2,444 endometrial were received during the 10-year study period constituting 12.2% of total specimens received at the Department within the study period. The age range of patients was 12-85 years with a mean age of 26 years. The peak age was between 30-39 years (Figure 1). The youngest patient presented with acute endometritis following septic abortion while the oldest patient presented with post-menopausal bleeding due to simple endometrial hyperplasia.

The functional endometrial changes were the most common histopathological diagnostic category, accounting for 53.8% (1035) of cases with secretory phase endometrium accounting for 941 (71.5%) of the functional changes (Figure 2), proliferative phase 296 (22.5%), and hormonal imbalance 39 (3%) of the cases respectively (Table 1). Acute and chronic endometritis accounted for 7.8% of all endometrial biopsies. Granulomatous endometritis constituted 0.2% of the cases. (Figure 3). Endometrial hyperplasia was diagnosed in 164 (6.7%) of the patients consisting of 143 (87.2%) cases of simple hyperplasia (Figure 4), 2 cases (1.2%) of complex hyperplasia and 19 cases (11.6%) of atypical hyperplasia. The age range of patients with endometrial hyperplasia was 14-85 years with an average age of 45 years. A total of 32 endometrial polyps and 3 papillary adenofibromas were diagnosed which together made up 1.4% of endometrial biopsies. Benign gestational trophoblastic disease was diagnosed in 108 patients (4.4%) and this comprised 56 (1.4%) partial hydatidiform moles and 52 (1.3%) complete hydatidiform moles (Table 1). The age range of patients with hydatidiform mole was 18-38 years with an average age of 28 years. The frequency of hydatidiform mole was 1 per 33
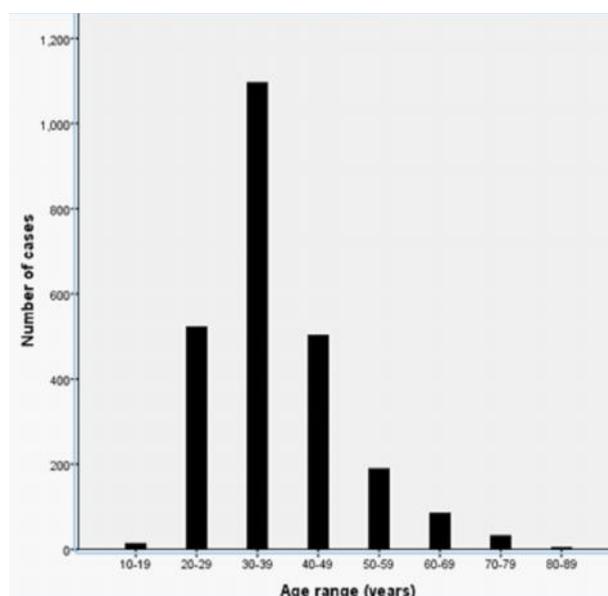

Fig. 1: Age distribution of 2,444 patients with endometrial biopsies

Table 1: Histopathological diagnosis of 2444 endometrial biopsies

DIAGNOSTIC CATEGORIES	SPECIFIC HISTOLOGICAL DIAGNOSIS	NUMBER	%
FUNCTIONAL ENDOMETRIUM	Hormonal Imbalance	39	1.6
	Menstrual phase	39	1.6
	Proliferative phase	296	12.1
	Early secretory phase	165	6.7
	Mid secretory phase	207	8.5
	Late secretory phase	569	23.3
	Subtotal	**1315**	**53.8**
ENDOMETRIAL ATROPHY INFLAMMATORY	Endometrial atrophy	**215**	**8.8**
	Acute endometritis	59	2.4
	Chronic non-specific endometritis	123	5.0
	Granulomatous endometritis	10	0.4
	Subtotal	**192**	**7.8**
ENDOMETRIAL HYPERPLASIA	Simple hyperplasia	143	5.8
	Complex hyperplasia	2	0.1
	Atypical hyperplasia	19	0.8
	Subtotal	**164**	**6.7**
BENIGN NEOPLASTIC LESIONS	Endometrial polyp	32	1.3
	Papillary adenofibroma	3	0.1
	Partial hydatidiform mole	56	2.3
	Complete hydatidiform mole	52	2.1
	Subtotal	**143**	**5.8**
MALIGNANT LESIONS	Epithelial tumours	65	2.6
	Stromal tumours	5	0.2
	Mixed tumours	10	0.4
	Other malignant tumours	2	0.1
	Choriocarcinoma	14	0.6
	Subtotal	**96**	**3.9**
MISCELLANEOUS UNSPECIFIED	Endometrial ossification	11	0.5
	Inadequate/Unrepresentative	310	12.7
GRAND TOTAL		**2444**	**100.0**

endometrial biopsies. Malignant neoplasms were diagnosed in 96 patients (3.9%) and these comprised 38 (1.5%) epithelial neoplasms, 5 (0.2%) stromal tumours, 10 (0.4%) mixed tumours, 14 (0.6%) choriocarcinoma and 27 (1.1%) secondary neoplasms (Table 1). The secondary neoplasms were cases of metastatic squamous cell carcinoma from the cervix, with an age range of 25 to 80 years and a mean age of 56 years.

The age range of patients with malignant epithelial neoplasms was 25-80 years with an average age of 55 years. Endometrioid adenocarcinoma (Figure 5) and serous adenocarcinoma accounted for 16.7% (n=16)

and 15.6% (n=15) respectively. The ages of these patients ranged from 57 to 75 years, with a mean of 67 years. There were 14 cases (14.6% of malignant neoplasms) of choriocarcinoma histological type. The ages of these patients ranged from 20 to 48 years with an average age of 31 years. Malignant mixed Müllerian tumours accounted for 10.4% of cases (n=10). The ages of these patients ranged from 45 to 70 years, with a mean age of 56 years. Six (60%) of these tumours were homologous and four cases (40%) had heterologous components. Stromal sarcoma accounted for 5.2% (n=5) of cases. All of these cases were high-grade neoplasms. The ages of the patients with stromal sarcoma ranged from 26 to 70 years with
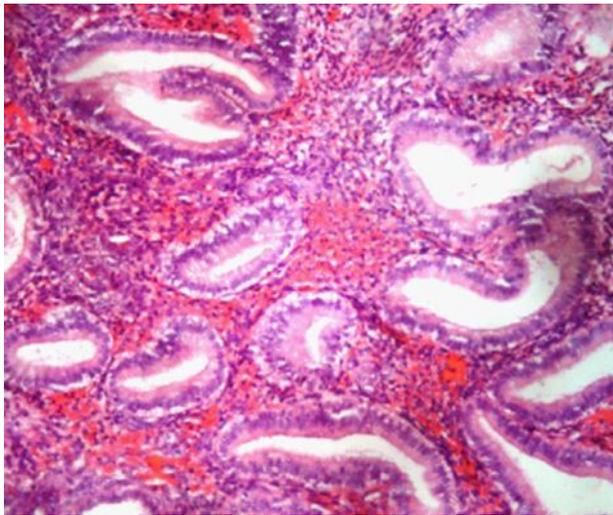
Fig. 2: Photomicrograph showing a case of secretory phase endometrium having irregular endometrial glands with subnuclear and supranuclear vacuolations (Haematoxylin and eosin, X200)
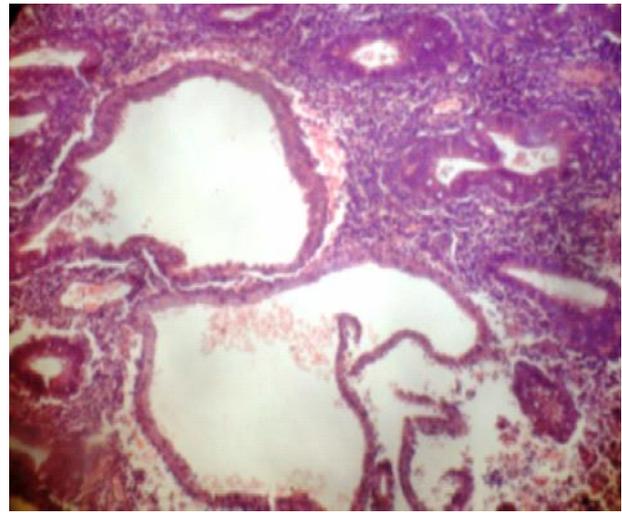

Fig. 4: Photomicrograph showing a case of simple endometrial hyperplasia having endometrial glands proliferation with accompanying cystic dilatation and lined by simple columnar epithelium. (Haematoxylin and eosin, X200)
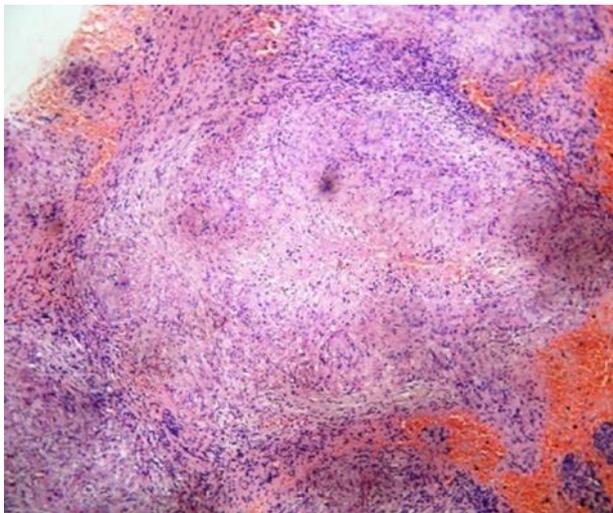

Fig. 3: Photomicrograph showing a case of granulomatous endometritis having focal accumulations of epithelioid cells, surrounded by a rim of lymphocytes and fibrosis (Haematoxylin and eosin, X200)
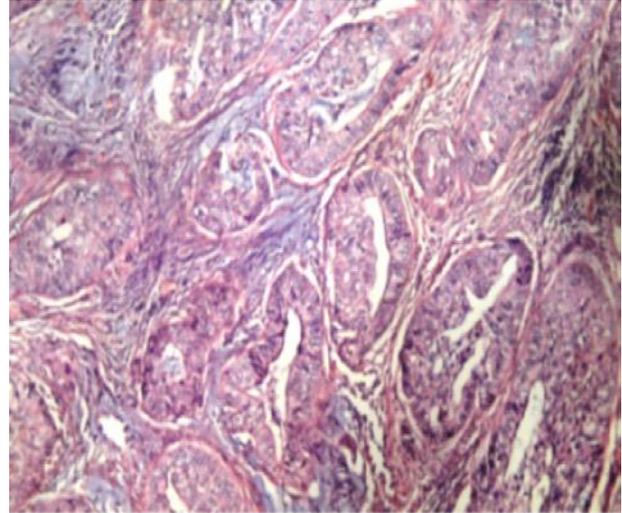

Fig. 5: Photomicrograph showing a case of endometrioid adenocarcinoma with endometrioid glands disposed in back to back and lined by malignant epithelial cells with desmoplastic stromal invasion. (Haematoxylin and eosin, X200)

a mean age of 48 years. A diagnosis of embryonal rhabdomyosarcoma was made in one patient aged 20 years, which was confirmed in the subsequent hysterectomy specimen.

Post-menopausal and abnormal uterine bleeding were the usual presenting symptoms in patients with malignant neoplasms. The relative frequency of primary endometrial malignant neoplasms was 1 per 25 biopsies and 1 per 8 endometrial biopsies in patients presenting with abnormal uterine bleeding and post-menopausal bleeding respectively.

DISCUSSION

In the present study, endometrial biopsies accounted for 12.2% of the total biopsies received at the Pathology Department in the period under review. This is very low compared to the previous 5-year study in Ibadan in which endometrial biopsies accounted for almost 50% of the total biopsies.[10] This decline could be partly due to adequate selection of patients for endometrial biopsy as part of investigation for infertility and other gynaecological symptoms. The value obtained in this study is however relatively the same compared to the findings in previous studies

from Lagos, which revealed that endometrial biopsies accounted for 11% of all the surgical biopsies.[8] This finding is however higher compared to studies from Jos which recorded endometrial biopsies as constituting 7% of all surgical biopsies submitted to the department.[5] The most common histological diagnostic category was functional endometrium, accounting for 53.8% of the cases. This is similar to previous studies from Maiduguri (55.7%),[7] Lagos (50.9%),[8] Ilorin (67.6%)[9] and Ibadan (72.8%),[10] which also showed predominantly normal functional endometrium. However, in a study from Jos, functional endometrium accounted for only 9.4% of endometrial biopsies[5]. The decline is partly due to inclusion of products of conception as part of Jos study which accounted for 54.3% of endometrial biopsies.[5]

Altogether, acute and chronic endometritis accounted for 7.8% of cases in the present study. This is relatively in agreement with the figures of 7.4%, 7%, and 8.8% respectively reported in previous studies from Ibadan,[10] Jos,[5] and Lagos.[8] However, the finding is in contrast with the previous Maiduguri and Ilorin studies, which reported that endometritis accounted for 13.6% and 3.51%, respectively of endometrial biopsies.[7,9] A diagnosis of granulomatous endometritis most probably tuberculous was made in ten cases accounting for 0.4% of endometrial biopsies. This is surprisingly low for this environment especially with the surge in Human immune-deficiency virus (HIV) infection associated with tuberculosis and low socio-economic status of the people. This low rate is relatively in agreement with previous studies from Ibadan (0.49%)[10], Lagos (0.2%)[8] and Ilorin (0.1%),[9] but in contrast with the 1.2% rate found in Maiduguri.[7] The reported low incidence of endometrial tuberculosis may be because of under reporting due to inadequate tissue sampling and in addition, availability of other modalities for investigating tuberculosis such as Mantoux test, sputum AFB and culture and chest x-rays, which allows treatment to be instituted before the disease spreads to involve the uterus. Endometrial hyperplasia occurred in 6.7% of the endometrial biopsies reviewed in the present study. This is higher than the figures of 3.48% and 2.47% respectively, reported in the previous studies from Ilorin[9] and Ibadan.[10] By contrast, much higher figures of 29.8%, 17.5% and 9.1% respectively, have been reported in previous studies from Maiduguri,[7] Jos[5] and Lagos.[8] The majority of the cases of endometrial hyperplasia in the present study were classified as simple endometrial hyperplasia accounting for 87% of cases and this is in tandem with what was reported in different parts of the country and Africa[5,7,9]

Endometrial hyperplasia in patients investigated for infertility accounted for 3% of cases and all were simple endometrial hyperplasia. These findings are relatively closer to that of Kano (5.1%)[12] and India (5.5%)[13] and lower compared to previous studies from Lagos (7%),[8] Ilorin (17%),[9] and Enugu (20%).[6] The finding in this study is however relatively higher if compared to findings from Calabar which showed endometrial hyperplasia in infertile patients accounted for 0.7% of endometrial biopsies.[4]

In this study, gestational trophoblastic disease (GTD) altogether comprised 122 (5%) of the cases, with hydatidiform mole accounting for the majority (88.5%) of cases (comprising 45% partial mole and 43% complete mole while choriocarcinoma accounting for 11.5% of the cases of GTD). These figures are relatively lower than those from other studies in Nigeria. In Jos, the incidence of GTD was 12.2% of endometrial biopsies, with choriocarcinoma accounting for 14.7% of GTD cases.[5] In Ibadan,[10] Ilorin,[9] and Lagos,[8] the overall frequency of GTD was relatively lower, being 3.02%, 2.1% and 1.3% respectively of the cases of GTD. It has previously been reported that corpus uteri malignancies account for 5.3% of all female genital tract malignancies in Ibadan.[10] In the present study, malignant neoplasms accounted for 3.9% of all endometrial biopsies. This is in tandem with 3% reported from Ilorin[9] but significantly higher than the figure of 0.56% reported in a previous study from Ibadan[10] and 1.4% reported in a study from Lagos.[8] Other studies of endometrial diseases in some parts of Nigeria,[5,7,9] Zimbabwe,[14] Ghana,[15] and India[13] have also revealed low frequencies of endometrial cancer. Endometrial carcinoma accounted for 1.6% of endometrial biopsies and 38.4% of malignant neoplasm in this study. This low frequency of endometrial carcinoma is in keeping with the observation that the frequency of occurrence of endometrial carcinoma is much lower in African countries compared to temperate countries.[16] This low frequency of endometrial carcinoma may be explained by the fact that low grade endometrial hyperplasia is the most common pattern of endometrial hyperplasia seen and the likelihood of developing carcinoma in a patient with simple hyperplasia is quite low accounting for 1%.[17,18] In addition specimens are sent to the laboratory in the form of hysterectomy specimen rather than endometrial curettage, probably because of late presentation due to low level of awareness in our society and this may have been missed out in a biopsy thus partly explaining the low frequency of endometrial carcinoma from this study of biopsy specimens.

The peak age incidence of endometrial carcinoma in this study was in the 5th decade and the mean age was 55 years. This is in tandem with other African studies[4,6] but contrasts with study done in an industrialized nation, where mean age of 60 years have been reported.[19] In this study, eighty seven percent of cases were seen within the age bracket 50-70 years; this is in conformity to the fact that endometrial carcinoma predominantly develops after menopause. In this study, five cases of endometrial stromal sarcoma were documented accounting for 0.2% of all endometrial biopsies and 5.2% of malignant neoplasms. This low frequency of endometrial stromal sarcoma was also recorded in previous studies from Ibadan (0.06),[10] Maiduguri (0.4%),[7] and Jos (0.5%).[5] Eighty percent (80%) of cases occurred within the age bracket of 40-70 years. Ten cases of Malignant mixed Müllerian tumour (MMMTS) were diagnosed within the study period constituting 0.4% of all endometrial biopsies and 10.4% of malignant neoplasms. This is slightly higher if compared to the previous Ibadan study which recorded MMMTS as 0.01% of endometrial biopsies[10]. The increase could be due to increased awareness in the population and also a wider period of study. Metastatic squamous cell carcinoma from the cervix accounted for 1.1% of endometrial biopsies and 28.1% of malignant neoplasms. Similar results were also recorded from Ilorin and Jos which showed that metastatic squamous cell carcinoma accounted for 0.6% and 0.5% respectively, of endometrial biopsies.[9,5] The peak age of incidence was seen between the age brackets of 50-69 years. These findings are not surprising considering that carcinoma of the cervix is the commonest gynaecological cancer and the commonest cancer in females in Nigeria.[20]

CONCLUSION

In this present study, we conclude that, the functional endometrial changes account for the highest morphological patterns while malignant lesions account for the least pattern of the endometrial biopsies evaluated for etiological basis of infertility, uterine bleeding and menstrual disorders in Ibadan. This study revealed a reduction in the number of endometrial biopsies received in the Department of Pathology, University College Hospital, Ibadan, which might be partly attributed to a decline in the number of endometrial biopsies received for infertility evaluation. Howbeit, Infertility was the commonest indication for endometrial biopsies while the least common clinical indication were the menstrual disorders as revealed by the findings from this present study.

The limitation encountered in this study include the inability to locate the slides and blocks; and lack of sufficient clinical details for some of the cases which accounted for the non-inclusion of the affected cases in the study population. Thus, the diagnostic importance of endometrial biopsies lies in providing accurate and concise clinical information on the Histological Request forms by clinicians; this will go a long way in better management of patients.

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