

Histopathologic Analysis of Endometrial Biopsies in a Northern Nigerian Teaching Hospital

Murtala Abubakar, Balarabe Kabir, Almustapha Aliyu Liman, Sani Muhammed Shehu, Bilkisu Lawal Kankia¹, Anisa Yahya¹, Zainab Adamu Ali

Departments of Pathology and ¹Obstetrics and Gynaecology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

Abstract

Background: Endometrial biopsy is a reliable means of evaluating the physiologic and pathologic states of the endometrium. The aim of this study was to examine the histopathological pattern of endometrial biopsies as seen in Zaria, Nigeria and to compare the results with similar studies elsewhere. **Method:** A retrospective analysis was carried out based on the records of the Department of Pathology, Ahmadu Bello University Teaching Hospital, Shika, Zaria between January 2014 and December 2018. The neoplastic lesions were classified according to 2014 World Health Organization classification for endometrial neoplasms. **Results:** A total of 1518 endometrial tissue samples were analysed. Pregnancy related conditions (41.76%) and functional endometrial changes (27.24%) were the most common morphologic diagnostic category seen. Endometrial hyperplasia (7.13%) was the most common pathologic lesion diagnosed. Of the malignant endometrial tumours, endometrial carcinoma is the most common with 29 cases (58% of all malignant endometrial lesions). One Hundred and Nine cases (7.2%) of the total cases reviewed were found to be inadequate for histopathologic evaluation. **Conclusion:** Retained product of conception was the most common morphologic entity seen in endometrial biopsy in Zaria. The proportion of endometrial samples that are inadequate for histopathologic evaluation is high. There is a need, therefore, for retraining of staff and standardization of biopsy procedures.

Keywords: Biopsies, endometrium, morphology, Zaria

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INTRODUCTION

Endometrial biopsy provides a safe and cost-effective means of obtaining sample for the evaluation of a wide spectrum of endometrial conditions.^[1] The procedure has acceptable degree of sensitivity and specificity.^[1,2]

Endometrial biopsy enables morphologic assessment of a variety of endometrial conditions that may include functional changes; pregnancy-related states; inflammatory conditions; as well as benign, premalignant, and malignant lesions. Clinically, the leading indications for endometrial biopsies are abnormal uterine bleeding, assessment of infertility, and postmenopausal bleeding.^[3] These represent a significant proportion of all the presenting complaints during hospital consultations among women during all phases of their reproductive lives.

The aim of this study, therefore, was to characterize the histopathologic patterns of endometrial biopsies received at the pathology department of a tertiary hospital.

MATERIALS AND METHODS

This retrospective analysis was carried out based on the histopathological reports of endometrial biopsy samples received at the Department of Pathology, of a teaching hospital, in northern Nigeria, over a 5-year period (January 2014 to December 2018).

The cases of interest were extracted from the surgical daybooks of the years under review. Other relevant data were obtained from the pathology request forms filled by the attending physicians and copies of the pathology reports issued on all the cases. The corresponding glass slides and stored paraffin

Address for correspondence: Dr. Murtala Abubakar,
Department of Pathology, Ahmadu Bello University Teaching Hospital,
Zaria, Nigeria.
E-mail: abubakarmurtala2@gmail.com

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Table 1: Frequency distribution of the various morphologic diagnostic categories of endometrial biopsy

	PRE-MENO	PERI-MENO	POST-MENO	Total	Percentage
Functional changes					
Proliferative	106	21	1	128	8.40
Secretory	126	24	0	150	9.90
Atrophic	9	20	46	75	4.90
Hormonal imbalance	47	13	0	60	4.00
	288	78	47	413	27.20
Preg related conditions					
Products of conception	387	60	0	447	29.45
Decidual changes	107	47	0	154	10.14
Arias-stella reaction	31	7	0	38	2.50
	525	114	0	639	42.10
Inflammatory conditions					
Chronic non-specific	66	18	7	91	6.00
Granulomatous	4	2	1	7	0.46
	70	20	8	98	6.46
Endometrial hyperplasia					
Typical	13	22	38	73	4.81
Atypical	7	8	20	35	2.30
	20	30	58	108	7.11
Benign tumours					
Endometrial polyp	21	18	2	41	2.70
Adenomyoma	0	1	0	1	0.01
Partial mole	29	2	0	31	2.04
Complete mole	27	1	0	28	1.84
	77	22	2	101	6.59
Malignant					
Epithelial	4	5	20	29	2.00
Stromal	2	1	2	5	0.33
Mixed	0	1	8	9	0.59
Choriocarcinoma	4	3	0	7	0.46
	10	10	30	50	3.38
Miscellaneous	70	25	14	109	7.18
Total	1040	309	169	1518	100

Table 2: Distribution of Patients by menopausal status

Age Category	Frequency	Percentage
Pre-menopausal	1040	68.5
Peri-menopausal	309	20.4
Post-menopausal	169	11.1
TOTAL	1518	100

tissue blocks (in cases of missing slides) for all cases were retrieved from the archives. Reviews of the initial diagnoses in the daybook were made only if at least three of the four general pathologists in the research team agreed that the review was necessary. All slides examined were 3–5-µm-thick sections made from 10% formalin-preserved tissue, processed according to standard protocols and embedded in paraffin wax. The stains employed in all cases were of hematoxylin and eosin.

Cases for which both the glass slides and the tissue blocks are missing as well as those from hysterectomy specimens were excluded from the study.

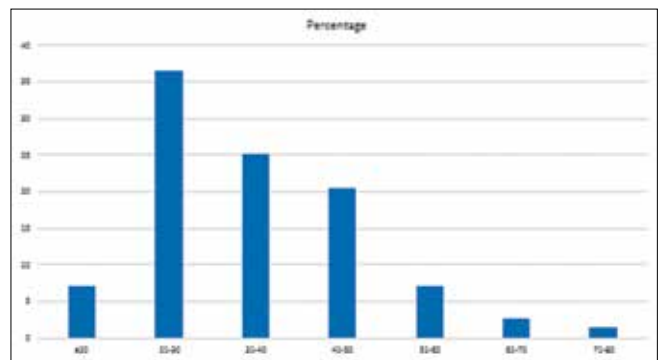


Figure 1: Age distribution of the patients

The neoplastic lesions were reclassified according to the 2014 World Health Organization classification of endometrial neoplasms.

The resulting data were analyzed using Microsoft Excel statistical package.

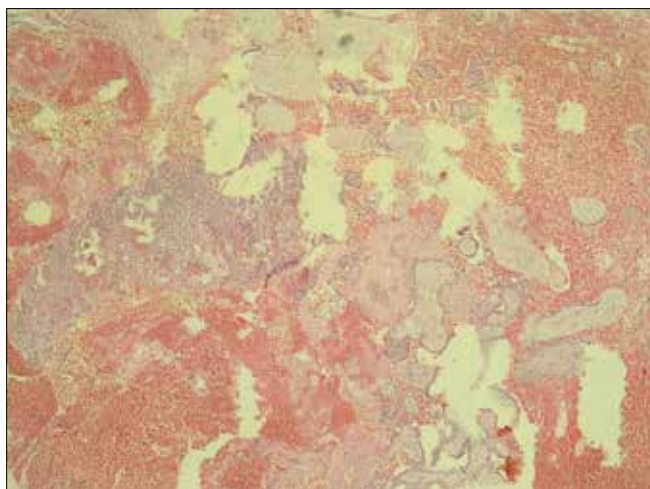


Figure 2: Photomicrograph of retained products of conception showing viable and ghosts of chorionic villi, hemorrhage, decidua, fibrin deposition, and necrosis

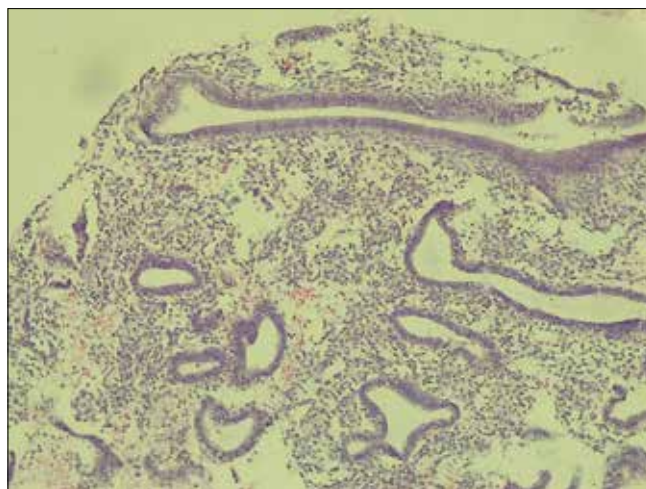


Figure 3: Photomicrograph showing secretory-type endometrial glands in an edematous, loose stroma

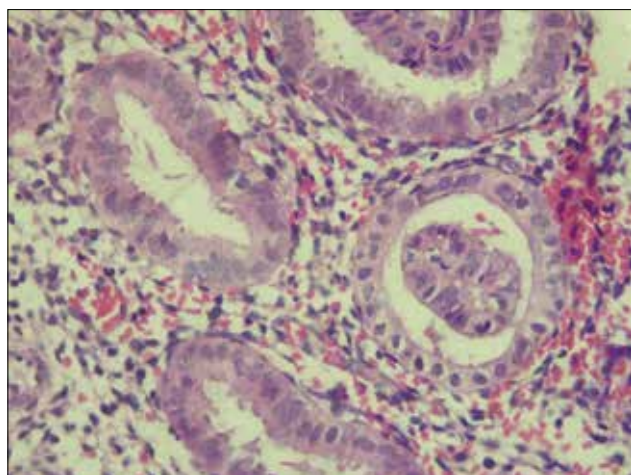


Figure 4: Photomicrograph of endometrial hyperplasia without atypia showing crowded endometrial glands lined by relatively bland pseudostratified columnar epithelial cells

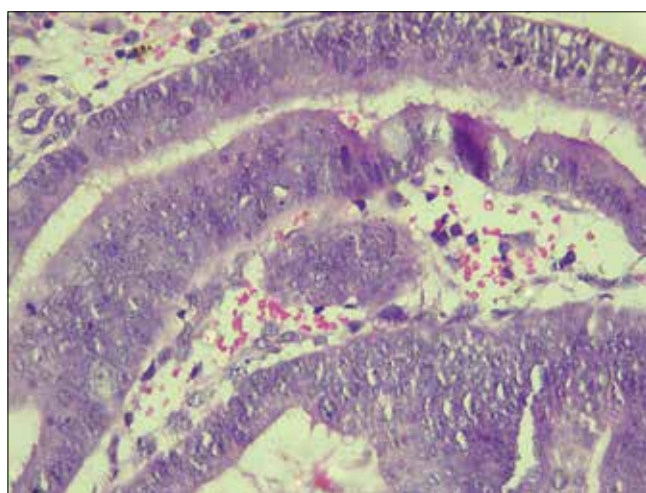


Figure 5: Photomicrograph of atypical endometrial hyperplasia showing crowded endometrial glands lined by cells exhibiting nuclear pleomorphism, hyperchromasia, and loss of polarity

Ethical clearance for the study was obtained from the Health Research Ethics Committee of the teaching hospital.

RESULTS

Endometrial biopsies constituted 9.2% (1518 of 16,500) of all specimens received in the laboratory over the 5-year study period.

The age range of the patients was 16–79 years, with a mean of 32 ± 7 years. The age range 21–30 years was, overall, the most common among our patients and constituted 36.4% (552/1518). Figure 1 shows the age distribution of the patients. The frequency distributions of the morphologic diagnostic categories are shown in Table 1. In Table 2, patients were categorized into premenopausal (<40 years), peri-menopausal (40–50 years), and postmenopausal (>50 years).

Pregnancy-related conditions were the most common histopathological diagnostic category, accounting for

42.1% (639) of cases. Retained products of conception (70%), was the most common morphologic entity under this category. Others in the category included decidual reaction (24%) and Arias Stella reaction (4%). These occurred mainly in patients aged 16–42 years, with a mean of 27 years. Figure 2 shows a typical case of retained products of conception.

The functional endometrial changes accounted for 27.2% (413) of cases. The mean age of these patients was 31 years. Under this category, secretory-phase endometrium accounted for 150 cases, whereas secretory endometrium and hormonal imbalances constituted 128 and 60 cases, respectively. Atrophic endometrial biopsy pattern was seen in 75 women, 61.3% of whom were postmenopausal. Figure 3 shows a photomicrograph of a typical case of secretory endometrium.

Inflammatory conditions involving the endometrium were diagnosed in 6.5% (98) of our cases. Nonspecific chronic

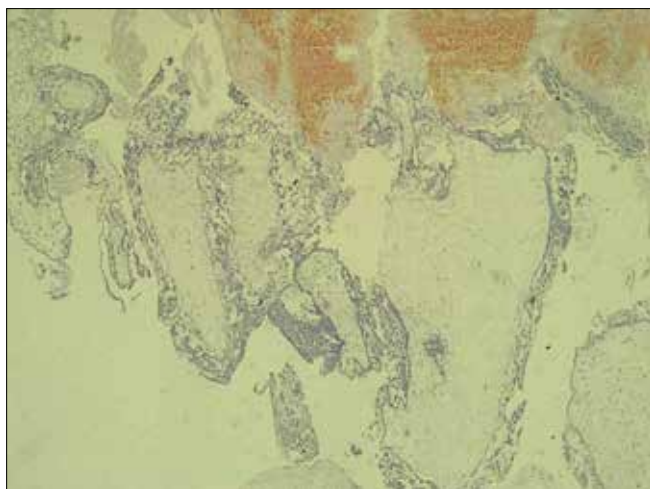


Figure 6: Photomicrograph of complete hydatidiform mole showing diffuse cystic enlargement and edema of chorionic villi and circumferential trophoblastic hyperplasia

endometritis accounted for 91 cases (6.0%), whereas granulomatous endometritis constituted 7 (0.04%) cases. Two (28%) of the cases of granulomatous endometritis stained positive for acid-fast bacilli (AFB) and were designated as tuberculous endometritis, while the remaining five tested negative for AFB and fungal stain (Grocott methenamine silver and periodic acid–Schiff).

Endometrial hyperplasia was the diagnosis in 108 (7.1%) of our cases. Approximately 2/3rd of these patients had benign hyperplasia, while atypical hyperplasia (endometrial intra-epithelial neoplasia) [Figure 4] was seen in 35 patients. More than half (53.7%) of the patients with endometrial hyperplasia were postmenopausal and their mean age was 49 years.

Benign endometrial tumors constituted 101 (6.7%) of all the morphologic entities seen in our study. Majority of these (59 cases) were gestational trophoblastic diseases comprising 31 partial [example shown in Figure 5] and 28 complete hydatidiform moles [example shown in Figure 6]. The mean age of patients with hydatidiform moles was 26 years. Nearly 95% of our patients with molar gestations were premenopausal, with the remaining 5% in their peri-menopausal years (40–50 years). Other benign endometrial tumors diagnosed included endometrial polyps (41 cases) and endometrial adenomyoma (1 case).

The malignant endometrial tumors seen in our patients included endometrial carcinoma (29 cases), malignant mixed Mullerian tumor (MMMT) (9 cases), choriocarcinoma (7 cases), and endometrial stromal sarcoma (5 cases). They altogether constituted 3.3% of the total endometrial morphologic entities seen. Sixty percent of the malignant lesions were seen in postmenopausal women. The mean age of the patients with endometrial carcinoma was 59.8 years. Endometrioid adenocarcinoma was the most common subtype (26 cases), while clear cell carcinoma and serous carcinoma had 2 and 1 case, respectively. Figure 7 shows a photomicrograph of a typical case of endometrioid adenocarcinoma.

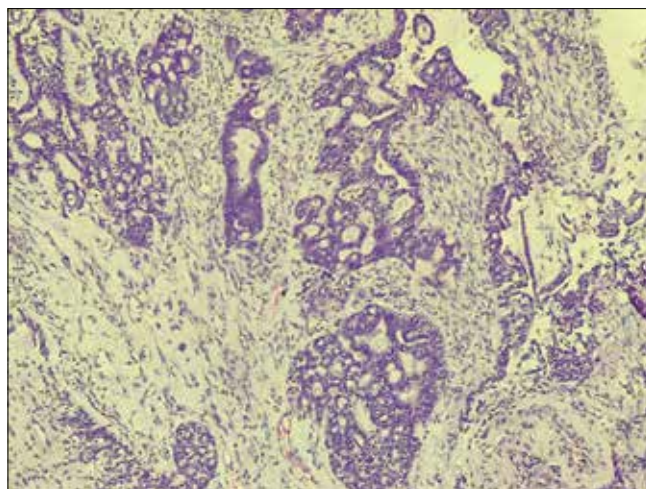


Figure 7: Photomicrograph of endometrioid adenocarcinoma showing fused, atypical endometrial glands with no intervening stroma

Choriocarcinoma was seen exclusively in the pre- and peri-menopausal age groups. The mean age of the patients with this condition was 29 years. The mean age of the patients with endometrial stromal sarcoma and MMMTs were 49 and 52 years, respectively. Postmenopausal bleeding (52%) was the most common presenting symptom in all malignant lesions of the endometrium among our patients.

DISCUSSION

In this study, endometrial biopsies constituted 9.2% of all surgical specimens received in our laboratory over the 5-year period. Other local studies have recorded about the same figures.^[4-6]

It is, however, considerably lower than a much older finding in Ibadan,^[7] South-western Nigeria, in which endometrial biopsies constituted about 50% of all surgical biopsies received over a 5-year study period. Factors that may explain the disparities include the inclusion of endometrial specimens obtained via hysterectomy in the Ibadan study, and the refinement of the selection processes of patients for endometrial biopsy (resulting into fewer women subjected to endometrial biopsies as part of evaluation for infertility and/or abnormal uterine bleeding) that may have occurred over the 25-year period between the two studies.

The age range (16–79 years), as well as the mean age (32 years) of patients undergoing endometrial biopsy in our study, is comparable to those found among women undergoing the procedure in Enugu, North-eastern Nigeria,^[8] and in a study from Pakistan.^[9]

Pregnancy-related conditions were the most common histopathological diagnostic category, accounting for 42.1% of our cases. Local studies by Dauda,^[6] Vhrithhire *et al.*,^[10] and Asuzu and Olaofe^[11] corroborated this finding. Other workers,^[4,12,13] however, found functional endometrial conditions as the most common morphologic category.

Variations in study methodology may be responsible for these differences. The latter studies have mostly excluded products of conception from their analyses.

Inflammatory conditions involving the endometrium were diagnosed in 6.5% (98) of our cases. Nonspecific chronic endometritis accounted for 91 cases (6.0%) of total endometrial biopsies, which agrees with the figures obtained from some local studies,^[4,5,7] while granulomatous endometritis constituted seven (0.5%) cases. The figure for granulomatous endometritis (which in our environment is considered to, most probably, result from disseminated tuberculosis) also agrees with other local data from Ibadan^[4] and Lagos.^[5]

Endometrial hyperplasia was seen in 7.1% of our study participants. This is close to the figures obtained in other centers in South-western Nigeria^[4,5] (6.7% and 8.1%). Studies from Jos^[6] and Makurdi^[7] (all in North-central Nigeria) reported higher proportions of endometrial hyperplasia among women who underwent endometrial biopsy (17.5% and 16.4%, respectively). This intra-country variation in the proportion of endometrial hyperplasia among women who underwent endometrial biopsy has also been noticed in India, where different authors reported significantly varied figures, such as Kau *et al.* (12%), Chitra *et al.* (16.2%), Kunda and Anupam (22%), and Soleymani *et al.* (2.5%).^[14-17] This probably reflects the influence of local/cultural practices related to excessive estrogen exposure on the etio-pathogenesis of endometrial hyperplasia.

Majority of cases of endometrial hyperplasia in our study were benign hyperplasia. This is similar to the findings of many other studies from within Nigeria, Africa, and other parts of the world.^[4,9,11,15,18]

In our study, hydatidiform mole constituted the majority of the benign endometrial tumors, and the ratio of complete to partial moles was almost 1:1. These findings are consistent with that of Abdullahi *et al.*^[4] and Vhritherhire *et al.*^[10] In addition, similar to our finding, a significant majority of patients with hydatidiform moles in the aforementioned studies were premenopausal.

Endometrial polyps constituted 2.7% of the entities seen among our patients. This is similar to the findings of Dike and Ojiyi,^[8] Abdullahiet *al.*,^[4] and Asuzu *et al.*,^[11] who reported a higher proportion of cases of endometrial polyp (9.9%) among women who had endometrial biopsy as part of evaluation for infertility. They postulated that it may be related to the ingestion of hormonal medications for the treatment of infertility.

Malignant endometrial tumors constituted 3.3% of the total endometrial morphologic entities seen in our patients, and a significant majority of these were seen in postmenopausal women with a mean age of 60 years. Similar patterns were reported from a prior study from our center^[15] from other parts of our country^[4,10,12] and from several other parts of Africa.^[18,19]

Endometrial adenocarcinoma was the most common of the malignant tumors constituting 58% of cases. Abdul *et al.*,^[20] Mordi and Nnatsu,^[21] and several other workers reported similar findings. Endometrioid adenocarcinoma constituted 90% of the histologic subtypes of endometrial carcinoma in our study. This is in tandem with the findings of other studies.^[4,8,10]

MMMT constituted 18% of all malignant endometrial lesions seen in our study. This figure has doubled what was found in a previous study in our center^[20] and also significantly higher than what was reported from Ibadan, South-western Nigeria.^[4] This may partly be due to exclusion of hysterectomy specimens from our study, which might have revealed malignant lesions other than MMT with consequent drop in the proportion of MMTs. Furthermore, the previous study has covered a longer period of time, which could result in it being more reflective of the real pattern.

In our study, five cases of endometrial stromal sarcoma were found. This represented 0.34% of all endometrial biopsies. Previous studies from our center,^[20] and others from Ibadan^[4] and Maiduguri,^[13] all in Nigeria, documented similar low frequency of occurrence of this tumor.

CONCLUSION

In this study, products of conception were observed to be the most common endometrial biopsy specimen received in our laboratory. The malignant lesions of the endometrium are more common among postmenopausal women.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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