



Original Article

Histopathological findings on endometrial biopsy in a tertiary care center of Nepal: a retrospective cross-sectional study

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ABSTRACT

Background: Abnormal uterine bleeding is the most common presentation in endometrial pathology and endometrial biopsy is the investigation of choice. This study aimed to describe the histological findings of patients who underwent endometrial biopsy to estimate the most common endometrial diseases in Nepali women.

Materials and Methods: This retrospective cross-sectional study was conducted using hospital records, and included females who underwent endometrial biopsy at a tertiary level hospital from 1 April 2018 to 31 March 2020. Histopathological findings were categorized into eight groups, and patients were divided into three age groups to obtain the relative occurrence of each type of disease at different ages.

Results: 342 female patients were included in the study, among which 97 were pregnancy-related and 245 were non-pregnancy-related. The mean age of the patients was 41.63 years (\pm 11.45 years). In 28 cases (8.2%) of the 342 total cases, the endometrial biopsy sample was deemed inadequate. Among the non-pregnancy-related cases, normal physiological changes were the most common reported finding (n=93, 38.0%), followed by abnormal physiologic changes (n=68, 27.8%). Premalignant conditions (n=15, 6.1%) and malignancy (n=5, 2.0%) were less common.

Conclusions: Normal physiological changes and disordered proliferative endometrium are the most common findings in an endometrial biopsy. Endometrial hyperplasia and malignancy are less common, and usually found in women more than 40 years in age.

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INTRODUCTION

Uterine endometrium undergoes cyclical changes under the influence of hormones like estrogen and progesterone. Any alteration in the normal physiology or organic causes may result in abdominal pain or abnormal uterine bleeding (AUB).¹ which is the most common presenting symptom in peri-menopausal or postmenopausal women, accounts for a large portion of the consultations in the Gynecological outpatient setup.^{2,3} AUB, defined as an alteration in the frequency, regularity, duration, and amount of blood flow, has a myriad of causes. Early in life, the cause is mostly functional. In women of the reproductive age group, the

cause can be pregnancy-related or infection/inflammation. Later in life, carcinomas must be ruled out.¹

A hysteroscopic biopsy is the standard diagnostic tool in patients presenting with symptoms suggestive of endometrial pathology. The endometrial sample assessed by light microscopy, sometimes with tissue stains, helps diagnose the cause of abnormal uterine bleeding, pelvic pain, or infertility.⁴ A biopsy can be performed in an outpatient setting.⁵ An adequate sample is obtained in more than 85% of the endometrial biopsy which can detect 87% to 96% of endometrial carcinoma.² Though uncommon, 25% of the cases of endometrial carcinoma occur in premenopausal women.⁶ Therefore, a biopsy should be performed in both premenopausal and postmenopausal if the degree of suspicion is high.

A wide range of endometrial histological findings is a diagnostic challenge. Endometrial pathology accounts for a large portion of gynecological patients in Nepal, however, it has not been studied extensively. The aim of the study was to investigate the histopathological findings of endometrium biopsy in women of all age groups presenting with various symptoms to the hospital, which will help estimate the most common endometrial pathologies in Nepali women.

MATERIALS AND METHODS

This is a retrospective cross-sectional study done in Shree Birendra Hospital, Kathmandu, Nepal, which is a tertiary referral center currently serving army personnel and their immediate family, as well as retired army personnel. Biopsy results from any female patient undergoing endometrial biopsy for any reason were included in the study. The endometrial tissues were either obtained from suction evacuation or curettage. The histologic findings of the endometrium obtained via hysterectomy were excluded from the study. The study includes patients who underwent endometrial biopsy from 1 April 2018 to 31 March 2020.

All endometrial samples included in the study were fixed in a 10% formalin solution after collection. They were later processed, slides were prepared and stained with hematoxylin and eosin, and examined via light microscopy by consultant pathologists.

Data were extracted regarding the demographic profile of the patient, indication for the biopsy, gross and microscopic findings of the biopsy, and the pathologist's opinion for each case from the records of the pathology department after obtaining appropriate authorization. The extracted data were filtered based on the inclusion and exclusion criteria using the Microsoft Office suite. The samples where there was no or little endometrial tissue present and the opinion by the pathologist was not possible were marked as "unsatisfactory". The histological findings of the remaining samples were categorized as follows: normal physiological changes which include proliferative, secretory, and

anovulatory endometrium; abnormal physiological changes which included hormone-induced changes (pill endometrium), irregular shedding, and disordered proliferative endometrium; inflammatory condition i.e., endometritis; benign condition, e.g., endometrial polyp; pre-neoplastic condition, including hyperplasia, with or without atypia; malignancy. Pregnancy-related changes were classified separately into categories of products of conception, molar pregnancy, decidual changes, and others.

Patients were divided into age groups of less than 40 years, 40-55 years, and more than 55 years, and the relative proportion of the different categorized findings were studied according to age groups. Statistical Package for the Social Sciences (SPSS) v. 25 was used for statistical analysis.

RESULTS

Within the study period of two years, a total of 342 cases were selected for evaluation of the histopathology of the endometrium. The age of the patients included in the study ranged from 19 years to 80 years with a mean age of 41.63 years (± 11.45 years). The indications for endometrial biopsy included abnormal uterine bleeding, especially perimenopausal and post-menopausal bleeding, suspected molar pregnancy, endometrial polyp, pregnancy complications, abortions, and bulky uterus. Among the 342 patients, 245 cases were non-pregnancy related. The remaining 97 (28.4%) underwent endometrial biopsy due to pregnancy-related indications. In 28 cases (8.2%) of the 342 total cases, the endometrial biopsy sample was deemed inadequate and no diagnosis could be reached.

The endometrial findings were stratified based on the age groups of the involved cases (Table 1). In the age group of < 40 years, the most common finding was pregnancy-related pathologies (95 cases) followed by normal physiological findings (23 cases). Malignancy was only noted in the age group more than 55 years (5 cases).

A normal endometrial epithelium was found in 93 (38.0%) of the 245 non-obstetric cases. Among them, details about the phase of endometrium were available in 84 cases (Table 2). Secretory endometrium was found in 34 cases (40.5%) and proliferative endometrium was noted in 41 cases (48.8%). Anovulatory endometrium was recorded in 7 cases (8.3%). Interval endometrium was seen in 2 cases (2.4%).

Abnormal physiological changes were noted in 68 of the 245 non-obstetric cases (27.8%). This included therapeutic hormone-induced changes in 8 out of 68 (11.8%) cases, irregular shedding and disordered proliferative endometrium in 37/68 (54.4%), asynchronous endometrium in 13/68 (19.1%), and stromal crumbling and breakdown 10 out of 68 (14.7%) (Table 3). Under inflammatory conditions, endometritis was noted in 18 of the 245 non-obstetric cases (7.3%). 18 cases (7.3% of non-obstetric cases) were categorized as benign conditions, all of which were cases of

Table 1: Endometrial patterns stratified based on age groups

Endometrial findings	<40 years (n)	<40 years (%)	40 to 55 years (n)	40 to 55 years (%)	>55 years (n)	>55 years (%)	Total (100%)	Percentage out of non-pregnancy related cases (n=245)
Normal physiological changes	23	24.73	66	70.97	4	4.30	93	38
Abnormal physiological changes	2	2.94	63	92.65	3	4.41	68	27.8
Inflammatory condition	4	22.22	12	66.67	2	11.11	18	7.3
Pregnancy-related condition*	95	97.94	2	2.06	-	-	97	NA
Benign condition	4	22.22	13	72.22	1	5.56	18	7.3
Pre-neoplastic condition	3	20.00	10	66.67	2	13.33	15	6.8
Malignant condition	-	-	-	-	5	100.00	5	2.0
Unsatisfactory sample	5	17.86	11	39.29	12	42.86	28	11.42
Total	136	39.77	177	51.75	29	8.48	342	

Table 2: Normal physiological spectrum in endometrial biopsy

Normal physiological findings	<40 years	40 to 55 years	>55 years	Total (n=84)
Proliferative	10	30	1	41
Secretory	9	24	1	34
Anovulatory	0	6	1	7
Interval endometrium	1	1	0	2

Table 3: Abnormal physiological changes observed in endometrial biopsy

Abnormal physiological changes	<40 years	40 to 55 years	>55 years	Total (n=68)
Hormone-induced	0	7	1	8
Disordered proliferative endometrium	0	36	1	37
Asynchronous	2	10	1	13
Stromal crumbling and breakdown	0	10	0	10

Table 4: Histopathological findings in the endometrial specimen in pre-malignant cases

Pre-malignant changes	<40 years	40 to 55 years	>55 years	Total (n=15)
Non-atypical endometrial hyperplasia	2	9	1	12
Atypical endometrial hyperplasia	1	1	1	3

an endometrial polyp.

The premalignant cases accounted for 6.1% (15 out of 245) of non-obstetric cases. Hyperplasia without atypia, present in 12 cases, was most common (Table 4). Malignant changes were noted in 5 cases, which is 2% of the non-obstetric cases.

The most common pregnancy-related pathology is retained product of conception seen in 53 cases, followed by decidual changes seen in 17 specimens (Table 5).

DISCUSSION

Endometrial biopsy is a widely used tool in the investigation of gynecological symptoms. Shree Birendra Hospital is a

Table 5: Pregnancy related endometrial findings

Pregnancy-related conditions	<40 years	40 to 55 years	Total (n=97)
Product of conception	52	1	53
Partial mole	5	1	6
Decidual changes	17	0	17
Hydropic abortus	2	0	2
Others	19	0	19

tertiary referral hospital in Kathmandu, Nepal. Patients visit the hospital from all areas of the country and it caters to a diverse group of individuals including active military personnel, their dependents, as well as retired military men and women. Therefore, the institution has a large catchment area with a diverse pool of patients. We could not study the indications completely due to incomplete recording in the pathology records, or possibly in the investigation forms themselves.

We categorized histopathological findings of the specimens into eight categories, similar to the study conducted by Baral and Pudasaini⁴, and the age of the patients into three groups for completeness and easy comparability. The age range of patients in our study who underwent endometrial biopsy was 19 years to 80 years. A study in Nepal has reported a similar age range of 27 to 70 years⁷ and another study describing the age range of 18 to 68 years.⁸

Normal physiologic changes: The endometrium is under the direct effect of estrogen and progesterone and changes with the rise and fall of these hormones. The proliferative phase is dominated by estrogen and the secretory phase is influenced by progesterone.⁹ In our study, normal physiological findings were common in the age group 40 to 55 years comprising 72.6% (61/84) of the total burden of normal physiological findings. The most common was proliferative endometrium, followed by secretory histological findings. Normal physiological changes were the most commonly seen finding in our study, which is consistent with the literature.⁴

Abnormal physiologic changes: Similar to a prior published study⁴, the most common age group experiencing abnormal physiological changes was the 40 to 55 years group. This might be attributed to the fluctuations in the hormonal levels as one approaches the menopausal state. Abnormal physiological changes accounted for 26.67% (80/300) of all endometrial findings in study⁴, whereas, it accounts for only 19.88% (68/342) of the cases in our study.

Endometritis: We report 5.3% (18/342) of inflammatory conditions with the major burden among the 40 to 55 years group. A study in Pakistan reported a 12% (28/241) burden of endometritis in a similar study.¹⁰ A study in Nepal reported the burden of 13.25% (22/166)⁷ whereas another reported the burden of 2.67% (8/300) which is lower than what we found.⁴

Benign condition: Benign endometrial polyps were found in 5.3% (18/342) of the cases in our study. Reported proportions in the literature range from 1.33% (4/300) of cases⁴ in a study in Nepal to 14% in a study from Pakistan.¹⁰

Pre-neoplastic condition: The pre-neoplastic conditions in our study accounted for 4.4% (15/342) of total biopsy results with the maximum burden found in the age group between 40 to 55 years. A study in Nepal found the pre-neoplastic burden to be 18.3% (55/300), which is much higher than what we reported, with the maximum burden lying in the peri-menopausal age group like our study.⁷ Another study from Nepal reported a 10.92% (44/403) burden of endometrial hyperplasia.¹¹ However, a study from Pakistan demonstrated a burden of endometrial hyperplasia as 5% (12/241), which is similar to our study.¹⁰ Differences in the baseline characteristics of patients visiting the hospitals, especially their age, could account for the differences seen among different studies in the literature.

The commonest finding was endometrial hyperplasia without atypia 80% (12/15) which occurred primarily in the age group between 40 to 55 years. Baral and Pudasaini also found endometrial hyperplasia without atypia to be the commonest form with 67.3% (37/55) of the hyperplastic cases.⁴

Neoplastic condition: Malignancy of the endometrium accounted for 1.5% (5/342) of the total samples in our study. A study in Nepal found adenocarcinoma in 2.41% (4/166) of cases, and another study showed 1% (3/300) of pathological examinations as malignant.⁷ Vaidya et al. reported a 2.48% (10/403) burden of endometrial carcinoma.¹¹ Similar to our finding, a study in Pakistan reported endometrial carcinomas 2% (5/241).¹⁰ As with premalignant conditions like endometrial hyperplasia, differences in patient characteristics could potentially account for this heterogeneity.

Pregnancy-related conditions: 28.4% (97/342) of the total samples yielded conditions resulting from pregnancy. It is much higher than reported in a study from Nepal with 5% (15/300).⁷ It was most commonly seen in the age group of < 40 years. The commonest form was the product of conception 54.6% (53/97) followed by others with 19.6% (19/97) and decidual changes 17.5% (17/97). The finding is similar to that reported in a Nepalese study with the commonest finding being product of conception 53.3%

(8/15).⁴ Partial mole accounted for 6.2% (6/97) of all pregnancy-related changes in the same study.

Unsatisfactory samples: Endometrial sampling through curettage or suction does not always yield sufficient endometrial tissue for analysis. Our study had 8.2% (28/342) of the samples which could not be diagnosed through histological examination. It is much higher than that reported from a similar study in Nepal with 4.22% (7/166) samples inadequate for evaluation⁷ but is similar to another study with a reported 8.3% (25/300) unsatisfactory samples.⁴ Another study in Nepal had a 5.9% (24/403) inadequate samples.¹¹

Overall, most of the findings in our study agree with most other published studies on the topic in the south Asian region. The relatively lower proportions of premalignant and malignant findings in our site could be due to the younger mean age of our patients. Our findings show that obstetric indications and findings account for a large proportion of endometrial biopsy, and while normal physiological changes are the most common findings, disordered proliferative endometrium, endometritis, and other pathologies are also commonly identified during the investigation of abnormal uterine bleeding and other gynecological symptoms.

CONCLUSIONS

Normal physiological changes and disordered proliferative endometrium are the most common findings in endometrial biopsy in our region of the world. Endometrial hyperplasia and malignancy are present in a smaller proportion of patients and are mostly found in women more than 40 years of age.

Conflict of interest: None

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