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Research Article

ORIGINAL RESEARCH ARTICLE: HISTOPATHOLOGICAL EVALUATION OF ENDOMETRIAL BIOPSIES IN WOMEN WITH GYNECOLOGICAL COMPLAINTS

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ABSTRACT

Objectives: The objectives of the study were to study histopathological evaluation of endometrial biopsies in women with gynecological complaints.

Methods: The present study included 100 patients who attended gynecology department of Dhiraj General Hospital, SBKS MI and RC with the complaints of abnormal uterine bleeding. Endometrial biopsy or curettage done by clinician as part of diagnosis and management. Samples sent to the department of pathology for histopathological evaluation. Tissue after appropriate fixation and processing was embedded in paraffin block. After that, 4 micron tissue sections were cut and they were stained with H and E stain. The sections were evaluated on microscopy and an appropriate histopathological diagnosis was made.

Results: Out of 100 cases studied, 37% were found out to be secretory endometrium, 20% proliferative endometrium, 6% disordered endometrial glands, 3% simple hyperplasia without atypia, 5% complex hyperplasia without atypia, 1% endometrial hyperplasia with atypia, 2% endometrial polyp, 7% chronic nonspecific endometritis, 1% tuberculous endometritis, 3% Arias-Stella reaction, 6% products of conception, 3% deciduitis, 1% complete hydatidiform mole, 2% endometrial carcinoma, and 3% squamous cell carcinoma of cervix.

Conclusion: Abnormal uterine bleeding is a leading cause of morbidity in patients with gynecological complaints. It not just impairing health but psychologically also affects the patients. Endometrial biopsy is a safe, reliable, and less time-consuming outpatient procedure which can be used as an initial diagnostic tool in the patients with abnormal uterine bleeding.

Keywords:

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INTRODUCTION

The endometrium which lines the uterine cavity is one of the most dynamic tissues in the human body; it is one of the interesting tissues for histopathologic study. It is characterized by cyclic processes of cell proliferation, differentiation, and death in response to sex steroids elaborated in the ovary. An understanding of the varieties in the normal morphological appearance of the endometrium provides an essential background for the evaluation of endometrial pathology [1].

Abnormal uterine bleeding is one of the most common problems in all age groups. The abnormal bleeding can be caused by a wide variety of disorders. It may represent a normal physiological state, and observation alone may be warranted. Alternatively, the bleeding can be a sign of a serious underlying condition necessitating aggressive treatment that could include a major procedure [2].

The causes for the bleeding in elderly women are hormonal, pregnancy complications, bleeding diathesis, and more importantly local pathology including malignancy, benign tumors, and infection. While dysfunctional uterine bleeding is responsible for most cases of abnormal uterine bleeding in the adolescent age group, the incidence of structural pathology increases in other age groups [3].

The bleeding in the perimenopausal period may be secondary to estrogen withdrawal (physiological state). In some cases, it may be due to malignancy of the reproductive organs, particularly in postmenopausal women.

The need to embark on a diagnostic curettage in perimenopausal women cannot be overemphasized [3].

It is now generally accepted that an adequate clinical examination of abdomen and pelvis, and uterine curettage, hysteroscopy, or at least an endometrial biopsy are essential to exclude organic disease of the uterus in these women [4].

The present study was carried out to find out the causes for abnormal uterine bleeding in women at Dhiraj Hospital and to compare the histopathological findings between the premenopausal and postmenopausal women.

METHODS

The present study was a prospective and observational (non-interventional) type of study, which included newly diagnosed patients of endometrial pathology selected from indoor and outdoor from obstetrics and gynecological department. A total 100 numbers of patients from January 2011 till December 2011 were recruited.

All endometrial biopsy specimens received in the Department of the Pathology, SBKS MI and RC, Vadodara, Gujarat, India, constituted the study material. The specimens were subjected to detailed histopathological examination. In each case, pathological reaction pattern was studied carefully and documented.

Brief clinical data were noted from the case records, which included the age, presenting symptoms, laboratory investigations, radiological investigations, and clinical diagnosis whenever available.

The inclusion and exclusion criteria for the present study were as follows:

Inclusion criteria

All types of endometrial biopsy sample were considered in this study.

Exclusion criteria

Inadequate biopsies and poorly preserved endometrial samples were excluded from the study.

The study was conducted on endometrial biopsy or D and C performed in hospital, in the best interest of patient. Hence, this study did not require any intervention to be conducted on patients. However, ethical committee clearance was obtained.

All the specimens were fixed in 10% formalin for 24 h after recording the gross morphological features – appearance, size, color, and consistency, and presence of necrosis/hemorrhage of endometrial tissue. A 5 mm thick bits or small tissue fragments aggregated and submitted for processing, 4–5 micron thick sections were cut with a microtome and stained with hematoxylin and eosin stain. The diagnosis of endometrial tissue was made on the basis of clinical presentation, gross morphology, and light microscopic features of H and E. Special stain, immunohistochemistry, immunophenotyping, and cytogenetic studies were not performed.

Table 1: Distribution of endometrial pathology in the present study

Endometrial pathology	No. of cases
Secretory endometrium	37
Proliferative endometrium	20
Disordered endometrial glands	6
Simple hyperplasia without atypia	3
Complex hyperplasia without atypia	5
Endometrial hyperplasia with atypia	1
Endometrial polyp	2
Chronic non-specific endometritis	7
Tuberculous endometritis	1
Arias-Stella reaction	3
Products of conception	6
Deciduitis	3
Complete hydatidiform mole	1
Endometrial carcinoma	2
Squamous cell carcinoma of cervix	3
Total	100

Table 2: Incidence of various causes of abnormal uterine bleeding

Cause	No. of cases
Benign non-organic cause	64
Benign organic cause	31
Neoplastic cause	5
Total	100

RESULTS AND ANALYSIS

In this study, spanning from January 2011 to December 2011; 100 cases of abnormal uterine bleeding were received in the Department of Pathology, SBKS MI and RC, Piparia, consisting of endometrial biopsies and curettings.

The following observations were made with regard to

The different endometrial patterns presenting as abnormal uterine bleeding in women were studied. Out of the 100 cases studied; the most common cause of bleeding was secretory endometrium, 38 out of 100 cases (38.0%). Proliferative endometrium was found in 20 out of 100 cases (20.0%); and disordered proliferative endometrium was 6 cases out of 100 (6.0%).

Simple hyperplasia without atypia was a cause in 3 cases out of 100 (3%) and complex hyperplasia without atypia was in 5 cases out of 100 (5%) followed by a 1 case out of 100 (1%) was endometrial hyperplasia with atypia.

Chronic non-specific endometritis presented as abnormal uterine bleeding in 7 out of 100 cases (7%). Endometrial polyp was a cause in 2 cases out of 100 (2%); and in 1 case (1%), tuberculous endometritis was a cause.

Products of conception 6 cases (6%) and Arias-Stella reaction and deciduitis were 3 cases each out of 100 each (3%) followed by 1 case (1%) of complete hydatidiform mole.

Among the malignant causes of abnormal uterine bleeding, the incidence was 2 of 100 cases (2.0%) which were endometrial carcinoma and other three cases of 100 were of squamous cell carcinoma of cervix.

Among the causes of abnormal uterine bleeding, benign causes had an incidence of 95% (95 cases out of 100) and neoplastic causes had an incidence of 5% (five cases out of 100). The malignant causes included 2% (two cases out of 100) of endometrial carcinoma and 3% (three cases out of 100) of squamous cell carcinoma of cervix.

In the present study, age of patients ranged from 20 years to 65 years.

In the age group of <30 years, the most common endometrial presentation with abnormal uterine bleeding was secretory endometrium in 10 cases followed by four cases of proliferative endometrium. There were

Table 3: Age-specific distribution of endometrial lesion in abnormal uterine bleeding

Endometrial pathology	≤30 years	31–40 years	41–50 years	>50 years
Secretory endometrium	10	16	10	1
Proliferative endometrium	4	7	8	1
Disordered endometrial glands	1	2	0	3
Simple hyperplasia without atypia	1	1	1	0
Complex hyperplasia without atypia	0	3	2	0
Endometrial hyperplasia with atypia	0	1	0	0
Endometrial polyp	0	1	1	0
Chronic non-specific endometritis	2	1	3	1
Tuberculous endometritis	1	0	0	0
Arias-Stella reaction	2	0	1	0
Products of conception	3	2	1	0
Deciduitis	2	1	0	0
Complete hydatidiform mole	1	0	0	0
Endometrial carcinoma	1	0	1	0
Squamous cell carcinoma of cervix	1	2	0	0
Total	29	37	28	6

three cases of products of conceptions and equal incidence of chronic nonspecific endometritis, Arias-Stella reaction, and deciduitis two cases each. Disordered proliferative endometrium, simple hyperplasia without atypia, tuberculous endometritis, and complete hydatidiform mole were observed in one case each. There were two cases with malignancy in this age group; one was endometrial adenocarcinoma and other was squamous cell carcinoma of cervix.

In the age group of 31–40 years, the highest incidence was of secretory endometrium; 16 cases; followed by proliferative endometrium seven cases. Disordered proliferative endometrium was observed in two cases. There were three cases of complex hyperplasia without atypia, one case of simple hyperplasia without atypia and endometrial hyperplasia with atypia each. One case of endometrial polyp and chronic non-specific endometritis was observed. Two cases of squamous cell carcinoma of cervix observed as a neoplastic cause. Two cases were of products of conception; one case of deciduitis.

In the age group of 41–50 years, there were totally 28 cases out of which 10 showed secretory endometrium, eight cases showed proliferative endometrium. Two cases showed complex hyperplasia without atypia with one case of complex hyperplasia with atypia. Chronic non-specific endometritis was observed in three cases, endometrial polyp was a cause in one case. Arias-Stella reaction and products of conception were observed in one case each. Endometrial carcinoma was a cause in one case in this age group.

In the age group of >50 years, there were only six cases which were observed. Three cases of disordered proliferative endometrium; one case of secretory endometrium and proliferative endometrium each observed in study. Chronic non-specific endometritis was observed in one case.

Majority of cases 48 were seen in the parity range of 3–4. Out of which 17 patients had secretory endometrium, nine had proliferative endometrium, six had chronic non-specific endometrium, four had endometrial hyperplasia, three had disordered proliferative endometrium, two had endometrial polyp, four had malignancy of which two were endometrial carcinoma and two of squamous cell carcinoma of cervix, and one each had Arias-Stella reaction and deciduitis.

Table 4: Relation of parity to endometrial histopathology

Endometrial pathology	0	1–2	3–4	>4
Secretory endometrium	2	17	17	1
Proliferative endometrium	0	10	9	1
Disordered endometrial glands	0	2	3	1
Simple hyperplasia without atypia	0	0	1	1
Complex hyperplasia without atypia	1	3	2	0
Endometrial hyperplasia with atypia	0	0	1	0
Endometrial polyp	0	0	2	0
Chronic non-specific endometritis	1	0	6	0
Tuberculous endometritis	0	1	0	0
Arias-Stella reaction	0	2	1	0
Products of conception	0	5	1	0
Deciduitis	0	2	1	0
Complete hydatidiform mole	0	1	0	0
Endometrial carcinoma	0	0	2	0
Squamous cell carcinoma of cervix	0	1	2	0
Total	4	44	48	4

Table 5: Distribution of endometrial hyperplasia in the present study

Endometrial pathology	No. of incidence	Incidence (%)
Simple hyperplasia without atypia	3	33.33
Complex hyperplasia without atypia	5	55.56
Simple hyperplasia with atypia	0	0.00
Complex hyperplasia with atypia	1	11.11
Total	9	100.00

In the parity range of 1–3, there were 44 cases (44.3%). Majority had secretory endometrium 17 cases. Ten cases had proliferative endometrium and five had disordered proliferative endometrium. Three had complex hyperplasia without atypia. One had tuberculous endometritis. Five cases had products of conception and two had Arias-Stella reaction and deciduitis each. One case had complete hydatidiform mole. There was single case of squamous cell carcinoma of cervix as a malignant cause of abnormal uterine bleeding.

In the parity range >4, there were four cases. Secretory endometrium, proliferative endometrium, disordered proliferative endometrium, and simple hyperplasia without atypia were a cause in one each.

There were four nulliparous women of which two showed secretory endometrium; and chronic non-specific endometritis and complex hyperplasia without atypia were a cause in one each.

Nine patients out of 100 with abnormal uterine bleeding had endometrial hyperplasia as the endometrial pathology. Out of nine cases, three were simple hyperplasia without atypia, five cases of complex hyperplasia without atypia, and a one case was of complex hyperplasia with atypia.

DISCUSSION

The present study was a prospective and observational (non-interventional) type of study. A total 100 numbers of patients from January 2011 till December 2011 were recruited. All endometrial biopsy and curetting specimens received in the Department of the Pathology, SBKS MI and RC, Piparia, constituted the study material. Microscopic study of the endometrial specimen is imperative for proper diagnosis and therapy of benign as well as malignant lesions.

Among 100 cases of endometrial biopsies analyzed in the present study, non-neoplastic cases were 95% and neoplastic cases were 5%. In the present study, we found that abnormal uterine bleeding presented with 64% benign non-organic cause, 31% benign organic causes, and 5% neoplastic cause.

In the present study, the patients of wide range in ages from 20 years to 65 years were observed. Mean age of the patients was 42.5±20.5 years. Maximum numbers (37%) of cases were seen in the age group of 31–40 years. Minimum numbers (6%) of cases were seen in the age group of more than >50 years.

Table 6 represents the summary of the different endometrial patterns reported by various authors. All the aforementioned studies have data with all causes of abnormal uterine bleeding and have shown their own respective incidences.

The highest incidence of secretory endometrium in the present study dealing with abnormal uterine bleeding (37%) was not observed in any of the previous studies. The study was done by Shaheen *et al.* [5] (2005), 33.91% which is comparable with our study.

In a study by Shazia *et al* . [6] (2010); 26.00% and by Dangal [7]; 10.70% had a lower incidence of secretory endometrium than the present study. The higher incidence of secretory endometrium in our study may be due to time of menstrual cycle when endometrial biopsy taken was later half of menstrual period according to clinical management of the patient.

Proliferative endometrium was found in 20.00% of cases in this study which correlated with the observation of Dangal [7] 17.80%. In the study conducted by Shaheen *et al*. showed 58.67% incidence and Shazia *et al*. [6] showed 33.00% incidence of proliferative which are higher

Table 6: Comparison of different studies with the present study

Name of study and sample size endometrial pathology	Greenwood and Wright [69] (1979) n=891	Dangal [70] (2003) n=84	Kuruvilla *et al.* [71] (2004) n=102	Shaheen *et al.* [72] (2005) n=121	Dreisler *et al.* [73] (2009) n=686	Shazia *et al.* [74] (2010) n=100	Baral and Pudasaini [75] (2011) n=300	Present study n=100
Age group	15–71 years	45–81 years	35–71 years	21–40 years	20–74 years	35–50 years	-	20–65 years
Secretory endometrium	63.00%	10.70%	50.90%	33.91%		26.00%	50.90%	37.00%
Proliferative endometrium		17.80%		58.67%		33.00%		20.00%
Disordered endometrial glands								6.00%
Simple hyperplasia without atypia	13.00%	10.70%	9.80%	4.95%		25.00%	9.80%	3.00%
Complex hyperplasia without atypia						1.00%		5.00%
Endometrial hyperplasia with atypia	2.00%							1.00%
Endometrial polyp	4.00%		7.90%	1.65%	7.80%		7.80%	2.00%
Chronic non-specific endometritis		6.00%				13.00%		7.00%
Tuberculous endometritis						1.00%		1.00%
Arias-Stella reaction	1.00%							3.00%
Products of conception							2.66%	6.00%
Deciduitis								3.00%
Complete hydatidiform mole							0.33%	1.00%
Endometrial carcinoma	2.00%	9.50%		0.82%		1.00%	1.00%	2.00%
Squamous cell carcinoma of cervix	-	-	-	-	-	-	-	3.00%
Other causes	6.00%	45.30%					25.60%	0.00%
Inadequate sample	9.00%		31.40%				1.91%	0.00%
Total	100.00%	100.00%	100.00%	100.00%	-	100.00%	100.00%	100.00%

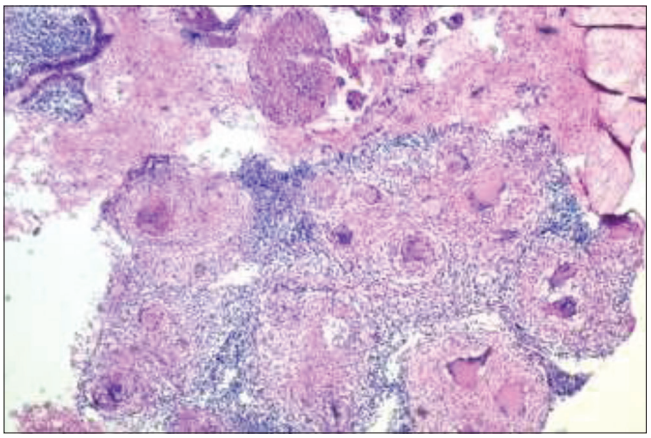

Fig. 1: Tuberculous endometritis – Tuberculous granuloma with endometrial glands and stroma (H and E, 10X)

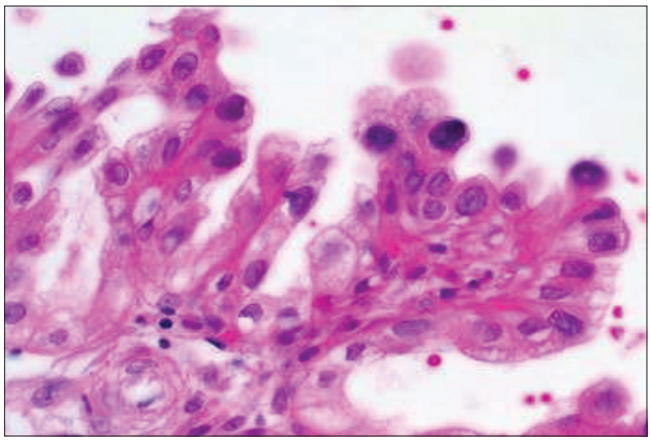

Fig. 3: Arias-Stella reaction – Hyperchromatic nuclei bulging into the lumen with cytoplasmic vacuolization (H and E, 40X)

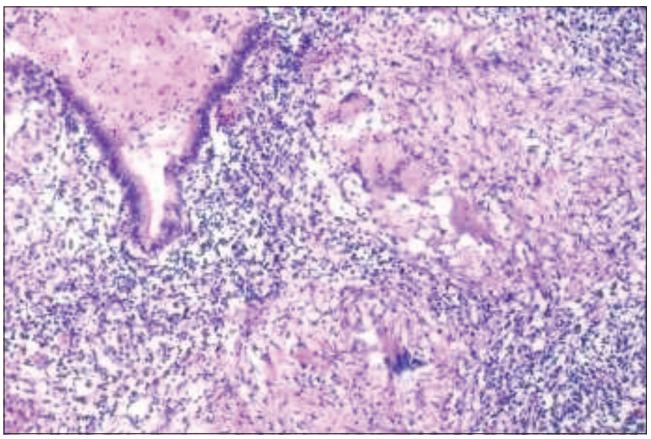

Fig. 2: Tuberculous endometritis – Langhans type of giant cells with endometrial gland and chronic inflammatory infiltrate (H and E, 20X)

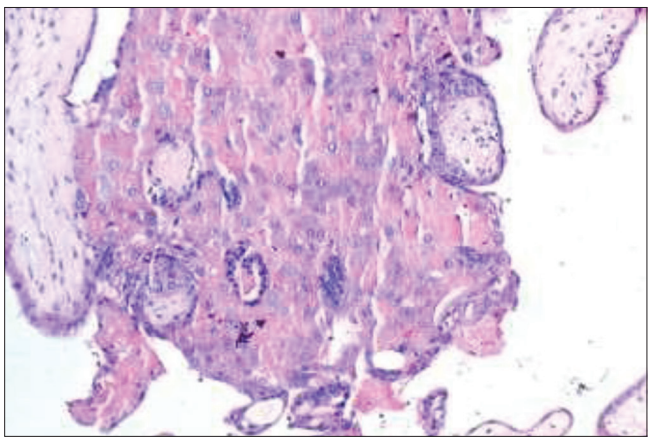

Fig. 4: Products of conception showing chorionic villi and trophoblastic tissue (H and E, 10X)

than present study. It may be because as part of clinical management patients had taken any external hormones or it can be a different time of menstrual cycle while taking endometrial biopsy.

In the present study, we have found 63% incidence in a group of proliferative endometrium, secretory endometrium, and disordered endometrial glands, which is comparable with the study of Greenwood

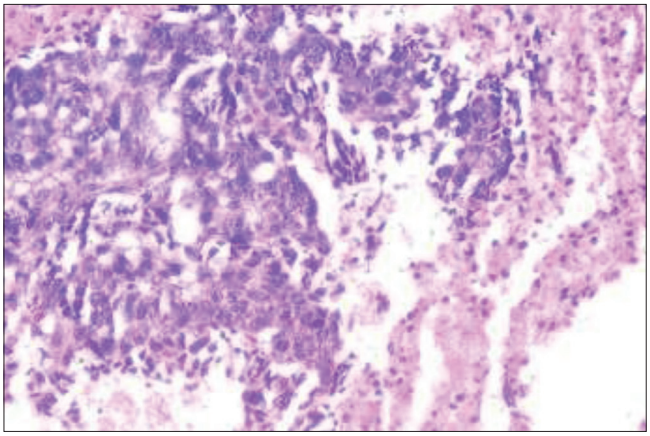

Fig. 5: Endometrial carcinoma – Tumor cells with high degree of pleomorphism, large nucleolus, prominent nucleoli, and mitotic figures, which are arranged in glandular pattern (H and E, 20X)

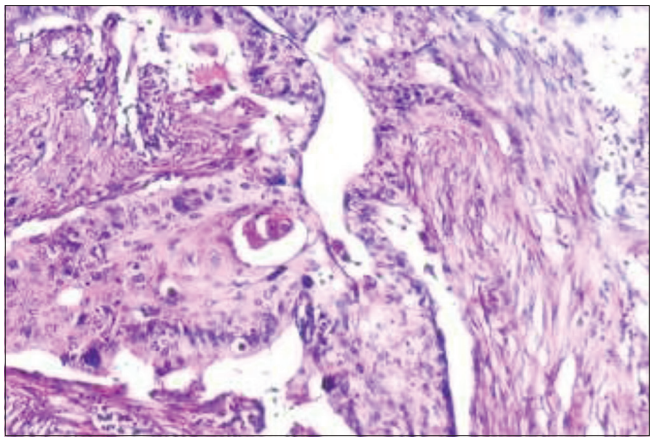

Fig. 6: Squamous cell carcinoma of cervix showing keratin pearl (H and E, 10X)

and Wright [8] with the same instances. Endometrial hyperplasia was found as a cause in 9% of abnormal uterine bleeding in the present study which is comparable with a study conducted by Dangal [7], 10.70%, Kuruvilla *et al*. [9], 9.80%, and Baral and Pudasaini [10], 9.80%. In the study by Greenwood and Wright [8], endometrial hyperplasia was observed in 15% of cases which is slightly higher than the present study.

In observation of study by Greenwood and Wright [8], there were 2% of cases of endometrial hyperplasia with atypia which is comparable within 1% of cases endometrial hyperplasia with atypia which were observed in the present study.

The incidences of endometrial polyp in the present study were 2%, which is comparable with the study of Shaheen *et al*. [5] with 1.65% incidence.

In the study of Greenwood and Wright [8] had 4.00% cases of endometrial polyp, Kuruvilla *et al*. [9] observed endometrial polyp in 7.90% cases. Dreisler *et al*. [11] observed 7.80% incidence of endometrial polyp and they noted that polyps were rare (0.93%) in the women below the age of 30 years and abnormal uterine bleeding was less frequent among women with polyps in comparison with other women.

Chronic non-specific endometritis was a cause of abnormal uterine bleeding in 7.00% of cases, which is comparable with the study of Dangal [7] with 6% of incidence. In the study of Shazia *et al*. [6], 13% of cases observed with chronic non-specific endometritis which is higher than the present study. Pelvic inflammatory diseases and sexually transmitted diseases may be responsible for higher incidence of endometritis in a study of Shazia *et al*. [6].

In the present study, there was a single case of tuberculous endometritis which is comparable with the study of Shazia *et al*. [6] where a single case of granulomatous endometritis was noted.

There were 13% of cases who were observed with pregnancy-related changes in women with abnormal uterine bleeding, which are higher than any other study. In the 1 year retrospective study of by Greenwood and Wright, it was 1.0%, and in the 3 year retrospective study of by Baral and Pudasaini [10], it was 2.66% only.

Statistical difference observed in comparison of pregnancy-related changes may be due to difference in the sample size, population, and duration and type of the study.

In the present study and a study done by Baral and Pudasaini [10], there was a single case of complete hydatidiform mole in each.

In the present study, there were 2% incidences of endometrial carcinoma observed which is comparable with other studies done by Greenwood and Wright [8], 2%, Shaheen *et al*. [5], 0.8% with Shazia *et al*. [6], and Baral and Pudasaini [10] observed 1.0% incidence. In the study done by Dangal [7], 9.50% of cases of endometrial carcinoma were noted which are higher than the present study, it may be due to difference in the parity and age at 1st pregnancy of the patient.

In our present study, an incidental finding of cervical squamous cell carcinoma was discovered. Kumaran *et al*. noted that in a patient with the complaints of abnormal uterine bleeding, suspicious of malignancy in the female genital tract should be considered even though it is uncommon. The three cases of cervical carcinoma were discovered in our study after D and C, though not suspected clinically.

CONCLUSION

Abnormal uterine bleeding is a leading cause of morbidity in patients with gynecological complaints. It not just impairing health but psychologically also affects the patients. Endometrial biopsy is a safe, reliable, and less time-consuming outpatient procedure which can be used as an initial diagnostic tool in the patients with abnormal uterine bleeding.

AUTHORS' CONTRIBUTION

All authors have equally contributed in this study.

AUTHORS' FUNDING

Nil.

CONFLICTS OF INTEREST

There were no conflicts of interest.

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