A STUDY ON ENDO MetriAL BiOPSIeS IN GYNaeCOLOGICAL SPECIMeN: A 2 YEARS RETROSPECTIVE STUDY
Satyasri Karri¹, Sweta Sinha², Kartheek B. V. S³

¹Associate Professor, Department of Pathology, RIMS, Srikakulam, Andhra Pradesh.
²Consultant, Department of Pathology, Indus Hospitals and Strand Life Sciences Private Ltd., Visakhapatnam, Andhra Pradesh.
³Consultant, Department of Pathology, Indus Hospitals and Assistant Professor, AMC, Visakhapatnam, Andhra Pradesh.

BACKGROUND
Uterine cavity is lined by the endometrial mucosa. Endometrium is continuously under hormonal effect throughout life. These hormones can be of ovarian or pituitary origin. Any alteration in the volume or pattern of menstrual blood flow is termed as abnormal uterine bleeding (AUB). Abnormal uterine bleeding occurring after one year of menopause is termed as postmenopausal bleeding (PMB). Pathology of endometrium can be better evaluated on endometrial biopsies, scrapings or curettage.

MATERIALS AND METHODS
The present study was a hospital based retrospective study carried out in a tertiary care hospital in coastal Andhra Pradesh. The materials for the study included endometrial curetting, scrapings, biopsies and hysterectomy specimens received between June 2016 and June 2018.

RESULTS
The present study constituted a total of 68 cases with age ranging from 28 years to 69 years. Two patients first underwent endometrial biopsy followed by total hysterectomy. These 04 specimens of two patients were taken as 02 cases only. All endometrial specimens were broadly classified into hyperplasias, benign and malignant. Each category was then sub-classified into specific types according to the current WHO classification (2014). Most common age group affected by all lesions was 51-60 years (25 cases) followed by 41-50 years (21 cases).

CONCLUSION
Abnormal uterine bleeding at any age can be alarming and should be evaluated thoroughly. As chances of tumours increases with age, even a minimal spotting in post-menopausal age should be taken seriously. Endometrial biopsy is the important test for the diagnosis of endometrial abnormalities; care should be taken in sampling. Inadequate or sampling from wrong site may lead to interpretation error.

KEYWORDS
Endometrial Biopsy, Abnormal Uterine Bleeding, Hormonal Effect.

HOW TO CITE THIS ARTICLE: Karri S, Sinha S, Kartheek BVS. A study on endometrial biopsies in gynaecological specimen: a 2 years retrospective study. J. Evid. Based Med. Healthc. 2018; 5(38), 2697-2702. DOI: 10.18410/jebmh/2018/553

ABSTRACT

Endometrial biopsy is the initial approach of choice for the patients with suspected endometrial hyperplasia or carcinoma. The aim of the
Aim and Objectives
The present study was done to categorize and evaluate the organic causes of endometrial abnormalities like hyperplasias, polyps and malignancies. All the functional causes like proliferative phase endometrium, secretory phase endometrium, pill endometrium and endometritis were excluded from the study. Inadequate biopsies were not taken for evaluation.

MATERIALS AND METHODS
The present study was a hospital based retrospective study carried out in a tertiary care hospital in coastal Andhra Pradesh. The materials for the study included endometrial curetting, scrapings, biopsies and hysterectomy specimens received between June 2016 and June 2018. The relevant clinical history and data were taken from the request forms. The haematoxylin and eosin (H and E) stained slides were retrieved and the slides were reviewed using light microscope under various magnifications, and the various histopathological findings were noted. Fresh sections were taken from tissue blocks in some cases, wherever required, and were stained with H and E stain. All the endometrial hyperplasia, polyps and carcinomas were studied in detail. Normal physiological endometrium, inflammation, drug induced changes and pregnancy related changes were excluded.

The various endometrium lesions were noted down. Various types of hyperplasias were classified as per WHO classification (2014), polyps and the tumours were classified according to WHO classification (2014). Data were then analysed using tables, figures and charts.

RESULTS
The present study constituted a total of 68 cases with age ranging from 28 years to 69 years. Two patients first underwent endometrial biopsy followed by total hysterectomy. These 04 specimens of two patients were taken as 02 cases only. All endometrial specimens were broadly classified into hyperplasia, polyps and carcinomas. Each category was then sub-classified into specific types according to the current WHO classification (2014).

In the present study, most common age affected were as follows (Refer Table 1)

- Hyperplasias- 41-50 years (21 cases),
- Polyps- 51-60 years (03 cases) and
- Malignancies- 51-60 years (09 cases)

Most common age group affected by all lesions was 51-60 years (25 cases) followed by 41-50 years (21 cases). Malignancies were not seen before 50 years of age.

Out of total 61 cases, hyperplasias were 42 cases, benign polyps 06 cases and malignancies 14 cases REFER CHART 1.
Clinically most common presentations were as follows:
- Abnormal uterine bleeding (AUB 34 cases) either menorrhagia or metrorrhagia,
- Uterine prolapse (02 cases) and
- Post-menopausal bleeding (PMB 32 cases).

Most common specimens were small biopsies (52 cases) either endometrial biopsies/ curettling/ scraping, polypectomy (03 cases) and total hysterectomy (13 cases). Out of all endometrial biopsies one case underwent fractional curettage.

**DISCUSSION**

The endometrial lining is divided into a deeper basal layer and a superficial functional layer. The superficial functional layer is under the influence of pituitary and ovarian hormones. Under the control of these hormones, endometrial lining undergoes proliferation, differentiation and shedding during the reproductive life. Any deviation from the normal menstrual cycle can be attributed to:
- Disorders of endometrial origin
- Disorders of hypothalamic-pituitary-ovarian axis
  - Female life can be divided into Reproductive (18-40 years), Peri-menopausal (41-50 years) and Post-menopausal (>50 years).

Minor variations of age can be seen in any of this category.

The most common organic presentation of abnormal uterine bleeding (AUB) in all age group is heavy bleeding, prolonged bleeding or spotting. AUB which presents as heavy or prolonged bleeding in reproductive period, acyclic flow in peri-menopausal period and minimal spotting at post-menopausal age is alarming and warrants evaluation to rule out malignancy. However cause of AUB can be related to patient's age as to whether the patient is pre-menopausal, peri-menopausal or post-menopausal.

Endometrial biopsy is mostly the first step of investigation for AUB. Histopathological evaluation of the endometrial biopsies plays an important role in diagnosing AUB. Earlier endometrial biopsies were taken by dilatation and curettage under general anaesthesia. Now-a-days it is done by Pipelle or other techniques in out-patient department. This newer technique has resulted in more inadequate/ scanty/ superficial biopsies as compare to older days. The job of pathologist has become tougher and at times frustrating. It is advisable to label endometrial biopsy as “inadequate” if there is no endometrial tissue and biopsies with superficial strips of endometrial glands should be labelled as “unassessable”.

Endometrial hyperplasia results from prolonged unremitting oestrogen stimulation. Rarely endometrial hyperplasia may present clinically as a polyp.

In WHO 1994 endometrial hyperplasia were classified as:
- Simple hyperplasia,
- Complex hyperplasia,
- Simple hyperplasia with atypia,
- Complex hyperplasia with atypia.

These categories in WHO '94 were descriptive whose interpretation didn’t suggest any specific management algorithms. In 2000 endometrial collaborative group (ECG) simplified the classification.

**ECG (2000) – EIN classification:**
1. Endometrial hyperplasia,
2. Endometrial intraepithelial neoplasia (EIN).

This EWG 2000 EIN system was accepted by WHO as an alternative to the WHO 1994 classification.

WHO published still simplified new classification of endometrial hyperplasia in 2014 by.

WHO 2014 endometrial hyperplasia classification (10):
- Non-atypical endometrial hyperplasia (benign hyperplasia)
- Atypical endometrial hyperplasia/ Endometrial intra-epithelial hyperplasia (EIN)/ Well differentiated carcinoma.

This new classification has made the pathology reporting a bit easier.

Mimickers of endometrial hyperplasia-
1. Artefacts
2. Cystic atrophy
3. Lower uterine segment endometrium
4. Disordered proliferative endometrium
5. Secretory endometrium or Arias–Stella effect
6. Benign papillary proliferations
7. Endometritis
8. Endometrial polyps

Care should be taken before diagnosing hyperplasia. The above-mentioned mimickers should be always kept in mind before making a final impression.
Figure 1. Photomicrograph showing endometrial hyperplasia without atypia. (A) Increased number of glands. (B) Gland with normal lining epithelium. (C) Gland in gland. (D) Cystically dilated glands. (H & E, 25X).

To differentiate between benign uterine lesions and atypical hyperplasia or EIN morphological criteria is taken which may be further supported by additional immunohistochemical (IHC) markers.

Endometrial polyps are growth of variable size projecting into the endometrial cavity. It may be asymptomatic or may present with AUB. Occasionally it may coexist with endometrial hyperplasia. But rarely secretory endometrium may present as a polypoid appearance. It may be seen with Tamoxifen therapy.

Figure 2. Photomicrograph showing squamous metaplasia (A) and endometrial hyperplasia (B) with atypia (C) (H & E, 25 & 40X).

Endometrial carcinomas can arise de novo or as a result of excessive oestrogenic stimulation and develop against the background of endometrial hyperplasia. Endometrial carcinomas are classified as WHO 2014. Histologic classification is as follows:

- Endometrioid adenocarcinoma and variants
- Mucinous adenocarcinoma
- Serous endometrial intraepithelial carcinoma (SEIC)
- Serous adenocarcinoma
- Clear cell adenocarcinoma
- Mixed cell adenocarcinoma
- Undifferentiated carcinoma
- Neuroendocrine tumours-
  - Well differentiated neuroendocrine tumor (carcinoid tumor).
  - Poorly differentiated small cell neuroendocrine carcinoma.
  - Poorly differentiated large cell neuroendocrine carcinoma.

Endometrioid adenocarcinoma is the most common type of endometrial carcinomas. The glands are well formed and resembles non-neoplastic glands. The nuclei are elongated and pseudostratiﬁed.

Endometrioid adenocarcinomas are divided into (FIGO grade):
- Well differentiated (grade I, < than 5% solid growth),
- Moderately differentiated (grade II, < than 50% solid growth),
- Poorly differentiated (grade III, > than 50% solid growth)

The most common differentiation associated with endometrioid adenocarcinoma is squamous differentiation.
Endometrial stromal tumours are rare. These tumours are more common in middle aged women.\(^1\)

Endometrial stromal tumors are divided according to the type of margins into:\(^3\)
- Benign (endometrial stromal nodule) - pushing margins
- Malignant (endometrial stromal sarcoma) - infiltrating margins.

WHO 2014 classifies endometrial stromal sarcomas into\(^12\):
- Low-grade stromal sarcoma- Cells resembling benign endometrial stromal cells with low/ high mitotic activity.
- High-grade stromal sarcoma- Cells are atypical resembling endometrial stromal cells but less atypical and pleomorphic than undifferentiated stromal sarcoma.
- Undifferentiated stromal sarcoma- Cells don’t resemble endometrial stroma. Marked atypia, bizarre and multinucleated cells, mitosis: 20/10 HPFs.

In the present study endometrial samples were derived from biopsy, curetting, scraping, occasional fractional curettage and hysterectomies. Endometrium was categorized as hyperplasia, polyp and carcinoma (both glandular and stromal).

Out of a total of 68 cases, most common age affected by hyperplasias were 41-50 years (21 cases) and polyps and malignancies were 51-60 years (03 cases and 09 cases respectively). Similar age group were affected by hyperplasias in study done by Sarika et al,\(^2\) Babbar et al\(^4\) and Ackerman also explains the same age group to be affected by endometrial hyperplasia.\(^1\)
Most common endometrial lesion was endometrial hyperplasias (71% of total cases). This is comparable to study done by Dipti et al\(^3\) (76%) and Nasira et al\(^6\) (84%). Out of the total 48 cases only 2 cases were seen with atypia.

Benign polyps were seen in total 6 cases (9%). Malignancies were seen in 14 cases (20%). This is comparable to study done by Dipti et al\(^3\) (24%) and Nasira et al\(^6\) (16%). Out of 14 cases of malignancies only 1 case was of stromal sarcoma. Most common type of carcinomas were endometrioid carcinoma.\(^3\)

**CONCLUSION**

Endometrial biopsies are one of the most common samples in histopathology reporting. Abnormal uterine bleeding at any age can be alarming and should be evaluated thoroughly. Endometrial hyperplasia is the most common organic lesion in peri-menopausal age. As chances of tumours increases with age, even a minimal spotting in post-menopausal age should be taken seriously. Post-menopausal bleeding should be considered as an indication of malignancy until proved otherwise by Dr. J. Glenn Bradley, still holds true. Although very rarely, other causes like pinworm infestation, genital tract tuberculosis and primary malignant melanoma of vagina has also been documented in literature.

Endometrial biopsy is the important test for the diagnosis of endometrial abnormalities; care should be taken in sampling. Inadequate or sampling from wrong site may lead to interpretation error.

**REFERENCES**


