

Histopathological Study of Endometrium in Abnormal Uterine Bleeding Patients in Tertiary Care Hospital of South West Bihar

Manjari¹, Rajendra Kumar²

¹PG Resident, Department of Pathology, Narayan Medical College & Hospital, Jamuhar, Rohtas District, Bihar, India

²Associate Professor, Department of Pathology, Narayan Medical College & Hospital, Jamuhar, Rohtas District, Bihar, India

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Corresponding author: Dr. Rajendra Kumar

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Abstract

Background: Endometrium is sensitive to sex hormones and abnormal uterine bleeding is prevalent in all age group females which cause anemia and affects quality of life. Pattern of endometrial pathology diagnosis is vital to know the proper cause of bleeding to maintain clinicians conversant in making their management strategy.

Methods: Study of endometrial biopsy was done retrospectively for a period of 1 ½ years. After processing of tissues, slides stained with hematoxylin & eosin by conventional method was examined microscopically. A statistical analysis between endometrial histopathology and mean age of presentation was done using Chi square test.

Results: After exclusion due to various reasons, 197 samples were enlisted for reviewing and final diagnosis was made. Endometrial hyperplasia emerged the commonest with 29.4% mostly in reproductive age group, followed by proliferative endometrium 20.3%, atrophy endometrium 16.24%, chronic endometritis 9.64%, endometrial polyp 8.63%, disordered proliferative endometrium 7.61% and secretory endometrium 6.6%. The endometrial carcinoma was diagnosed in only 1.52% of cases mostly in postmenopause females. The menorrhagia was the most common complaint overall (48.2%).

Conclusion: The D & C method is suitable but a newer technique has more scope. The commonest endometrial pathology in this study came out to be endometrial hyperplasia. For that unplanned use of hormone therapy is to be avoided.

Keywords: Endometrium, Abnormal uterine bleeding, endometrial carcinoma.

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Introduction

Endometrium is extremely sensitive part of female reproductive system to sex hormones. The clinical condition of abnormal uterine bleeding is an alteration of natural menstruation in reproductive age group, and after menarche bleeding per vaginum occurs due to hormonal imbalance. It is an irregularity in frequency,

volume and duration. It is associated with reproductive, iatrogenic and structural causes leading to a clinical entity of anemia which affects quality of life, and is already prevalent alarmingly in developing world [1].

Abnormal uterine bleeding (AUB) includes dysfunctional uterine bleeding (DUB) affecting mostly adolescent girls commonly related to anovulation and pregnancy complications, whereas atrophy and carcinoma related bleeding are common in older patients in addition to structural causes common in all age groups [2,3]. About 37% of teenagers have complications of abnormal uterine bleeding during first 3-5 yrs from menarche. It may be caused by even simple inflammation of endometrium. The commonest pathology irrespective of age group is disordered proliferative pattern [4,5]. Clinical conditions of obesity, hyperglycemia, hypertension, anovulation and oestrogen therapy has increased risk for hyperplasia favoring risk of cancer development. Mortality is increased in these cancer patients [3,6]. The FIGO has approved, a classification PALM-COEIN in 2011 in non-gravid female, is the recent classification for AUB.

For diagnosis of abnormal uterine bleeding, D & C sampling is adjudged as the gold standard. Other methods like saline infusion, sonography, 3D ultrasonography has become popular. D & C and hysteroscopy with dilatation of cervix require anesthesia which is cumbersome for both patient and gynecologists and this has given path to newer techniques like office hysteroscopy and vacuum devices averting anesthesia, and can be performed in outdoors cheaply and easily. However, histopathology constitutes the definitive diagnosis in all women with AUB that is unresponsive to medical and hormonal therapy [7]. Endometrial sampling for evaluation of infertility or preparation for in vitro fertilization related to AUB is important [8].

AUB varies upon geographical location and are usually 1/3rd gynecology cases in developing countries including India. Prevalence of AUB in Bihar has been reported 5-15% [9-12]. Evaluation of

samples related to AUB was performed in this institute for the first time to assess the frequency of endometrial histopathologic pattern in the present location of south-western Bihar, India.

Material & Methods

The present retrospective study was done in Pathology department of Narayan medical college & hospital, Jamuhar, Bihar, India. The cases were enlisted of 18 months from August 2019 to January 2020. The samples were received in the department for grossing and microscopic examination. Ethical approval of this project has been rendered by institutional ethics committee.

Inclusion Criteria:

This study includes samples of D & C, endometrial biopsy and hysterectomy cases sent mostly from Gynecology and obstetrics department related to abnormal uterine bleeding with proper clinical history.

Exclusion Criteria:

Samples improperly fixed,
Complaints of pregnancy related samples,
Acute pelvic inflammation samples,
Haemostatic disorder samples,
Specimens without proper history and
Autolysed specimens.

Under protocol of exclusion criteria, 31 samples were excluded and the specimens within above mentioned criteria came to be 197. The specimens were fixed properly in 10% formalin overnight. Gross examination under proper procedure was conducted, and details of important and abnormal findings were noted. Portion of curettage material and small tissue bits of biopsy were taken. It was processed properly in different dilution of alcohol. It was embedded in paraffin, and then sections of 4-6 micron were taken of paraffin blocks by semi-automated microtome. Sections were kept on glass

slide, and deparaffinisation done. The sections were then stained with Hematoxylin and Eosin by conventional method. Special stains were used as and when required. Microscopic examination was done by two pathologists individually, to reduce observer bias. The details of clinical history, age, parity, clinical complaint, menstrual and family history were retrieved from indoor records and histopathology requisition. The data was entered meticulously in MS Excel and a statistical analysis between age of presentation and specific endometrial causes was done using Chi square test χ^2 . P-value of 0.05 or less was considered statistically significant. Age was presented as mean \pm SD. Data was depicted in form of tables, graphs and photographs.

Results

The present study included 197 cases of endometrium with abnormal uterine bleeding, after elimination of thirty one samples due to various reasons of exclusion criteria.

There were 70 samples of D & C, endometrial biopsy and 127 hysterectomy samples. The cases ranged from 16 yrs to 84 yrs with mean age of 44.06 yrs \pm 11.1 SD. Most of the cases were in the range of 41-50 yrs (36%) followed by 31-40 yrs (29.4%). This is shown in **Table 1**. The cases were differentiated in various age groups in this table. The cases consisted of para 1-7 in this study. Para 1-2 (38%), para 3-5 (32%) and rest were evaluated in decreasing order of para 6 (23%) and para 7 (7%).

Table1: Showing distribution of cases in different age groups.

Age group	No. of cases	% of cases
<20 Yr	1	0.5
21-30 Yr	21	10.6
31-40 Yr	58	29.4
41-50 Yr	71	36
51-60 Yr	32	16.2
61-70 Yr	11	5.6
71 Yr & above	3	1.5
Total	197	100%

The overall histologic diagnosis of this series is depicted in **Table 2**. These were again specifically subdivided into three- reproductive (16- 40 yrs), perimenopausal (41-50 yrs) and postmenopausal (51 yrs and above) as shown in **Table 3** Postmenopause was considered as complete cessation of menstruation after 1 year of amenorrhea.

Table 2: Showing various histological diagnosis of endometrium in the study.

Endometrial hyperplasia	58	29.44
Proliferative endometrium	40	20.3
Atrophic endometrium	32	16.24
Chronic endometritis	19	9.64
Endometrial polyps	17	8.63
Disordered proliferative endometrium	15	7.61
Secretory endometrium	13	6.6
Endometrial carcinoma	3	1.52
Total	197	100%

Table 3: Showing endometrial findings in reproductive, perimenopausal & postmenopausal age groups.

Pathologic lesions	Reproductive age group	Perimenopausal age group	Postmenopausal age group
Endometrial hyperplasia	27 (33.75%)	20 (28.17%)	11 (23.91%)
Proliferative endometrium	18 (22.5%)	19 (26.7%)	3 (6.52%)
Atrophic endometrium	2 (2.5%)	10 (14%)	20 (43.47%)
Chronic endometritis	10 (12.5%)	6 (8.45%)	3 (6.52%)
Endometrial polyps	7 (8.75%)	8 (11.26%)	2 (4.34%)
Disordered proliferative pattern	9 (11.25%)	3 (4.22%)	3 (6.52%)
Secretory endometrium	7 (8.75%)	4 (5.63%)	2 (4.34%)
Endometrial carcinoma	0 (0%)	1 (1.4%)	2 (4.34%)
Total	80	71	46

The most common histopathologic pattern assessed in this study was of endometrial hyperplasia in 58/197 samples (29.4%). This consisted of 45 samples without atypia and 13 cases with atypia. Endometrial hyperplasia was most common in reproductive age group consisting of 27/80 cases (33.7%) and that of perimenopausal in 20/71 cases (28.2%). Proliferative endometrium finding of 20.3% was most common in perimenopausal age group (26.76%).

Atrophic endometrium was evaluated in 32 cases (16.2%) and it came out to be most common in postmenopausal age group (43.47%) followed by perimenopausal age group (14.08%). whereas chronic endometritis cases were diagnosed in 19 samples (9.64%). The commonest finding was ascertained in reproductive age group (12.5%) followed by perimenopausal group. One case was found to be of mixed infection in a 70 yr debilitated female. Endometrial polyp was diagnosed in 17 cases with highest no. of cases in

perimenopausal and reproductive age group (11.26% and 8.75% respectively).

The disordered endometrium was found in 15 cases (7.61%). It was also found commonest in reproductive age group followed by 3 cases each in both perimenopausal and postmenopausal. Other histologic pattern diagnosed was of secretory endometrium (6.6%) in 13 cases.

The least no. of diagnosis was made of endometrial carcinoma in 3 samples (1.52%) all involving above 50 yrs of age in this mission. Papillary variant was seen in 2 cases of 50 yr and 56 yr females including later with complaint of heavy bleeding. **Figure 1** shows multiple papillary structures lined by malignant cells in a 56 yr female. A third case of 62 yr female sample was diagnosed as moderately differentiated adenocarcinoma with gland as well as solid patterns (**Figure 2**). A comparison of endometrial diagnosis for AUB in this study with other studies is represented in **Table 4**.

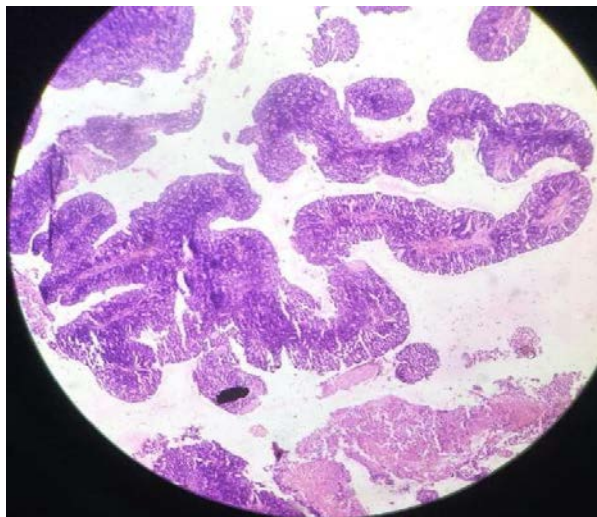


Figure 1: Showing multiple papillary structures lined with atypical malignant cells in a 56 yr. female.

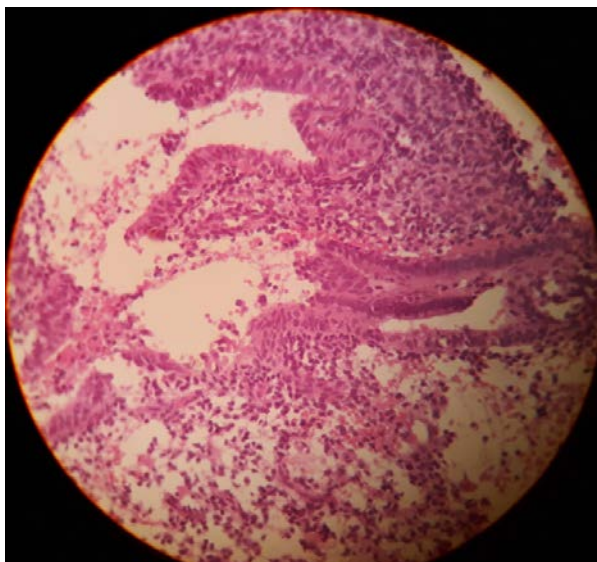


Figure 2: A 62 yr female sample was diagnosed as moderately differentiated adenocarcinoma with gland and solid patterns

Table 4: Showing comparison of endometrial diagnosis with other studies.

Endometrial diagnosis	Present study (n= 197)	Sajitha et al [3] (n= 156)	Doraiswami et al [5] (n= 409)	Abid et al [10] (n= 241)
Endometrial hyperplasia	29.44%	25%	6.10%	5%
Proliferative endometrium	20.30%	12.20%	-	13.70%
Atrophic endometrium	16.24%	5.10%	2.40%	6%
Chronic endometritis	9.64%	0.60%	4.10%	12%
Endometrial polyps	8.63%	5.10%	11.20%	14%
Disordered proliferative pattern	7.61%	12.20%	20.50%	27%
Secretory endometrium	6.60%	16.70%	-	20.30%
Endometrial carcinoma	1.50%	4.50%	4.40%	2%

The clinical complaint is portrayed in **Figure 3**. The most common complaints of AUB was encountered of menorrhagia in 47.8% patients followed by metrorrhagia in 22.4% cases mostly in reproductive and then perimenopausal age groups. Intermenstrual bleeding was associated

with 12% patients and polymenorrhea in 6.5% cases dispersed in almost all groups. Among postmenopausal patients, abnormal bleeding was evaluated in 11.3% cases. Endometrial causes of AUB and their average age pattern was statistically significant with P value <0.05.

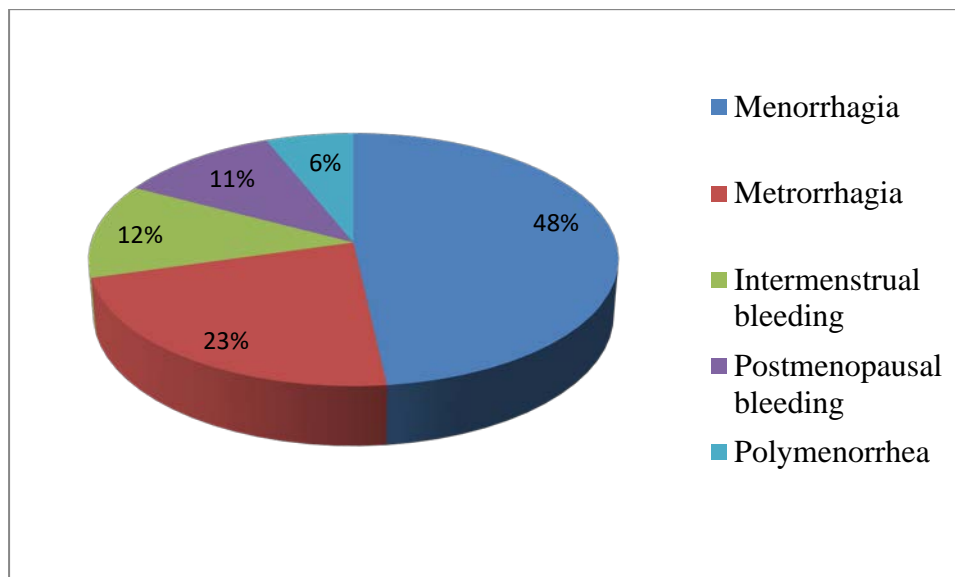


Figure 3: Showing different types of bleeding pattern in the study.

Discussion

Abnormal uterine bleeding complaint is a major health problem among females especially in developing nations. A chunk of general female population suffers from anemic condition. The management of these patients becomes a challenging task for gynecologists. Research is going on for detecting more accurate cause of AUB. Alteration of bone morphogenetic protein (BMP) expression has been found in patients with AUB and BMP7 will be a promising target for future investigation and treatment [13].

The study was conducted to know the prevalence of endometrial lesions and thereby suitable preventive as well as treatment measures is assured. The most common age group 36% (41-50 yr) recorded in this study resembles with the findings of one study [5], whereas, some other studies also recorded highest no. of

cases in the same age group in their studies [11,14].

Endometrial hyperplasia emerged as the commonest lesion (29.4%) in this study. Complex hyperplasia with atypical change, when progesterone level sustains at higher level, can transform into endometrial carcinoma in about 8-30% cases if not managed in time. Thus hormone therapy is a risk factor for its development. In a study it was recorded 25% [3]. In a study it was diagnosed in 6.1% cases. This may be due to geographical variation [5].

Proliferative endometrium, is influenced by imbalance of sex hormones, was diagnosed 20.3% next to endometrial hyperplasia in this series. Various scientists accounted 13.7 %, 20.5% and 37% in their studies [5,10,11]. Proliferative endometrium was also observed the most common among AUB patients in another study [14]. Atrophy endometrium is a natural age

related process involving usually menopausal females but nutritional factor may also be responsible among perimenopausal age group. Cystic or tubular glands and inactive collagenised stroma were the points of diagnosis. The evaluation of atrophy endometrium was 16.2% in the present study. It was diagnosed as low as 1.3% in a study to 24.5% in another study in the same country [15,16]. Chronic endometritis has a possible relation to infertility, and socio-economic condition is a definitive risk factor for its development. It is a common cause of vaginal discharge. Hence, endometritis should be kept in mind during evaluation [7]. Prevalence of 10-11% in general population has been documented. These cases were ascertained in this series in 19 patients (9.6%). Chronic endometritis was diagnosed 3.28%, 4.1% and 12% in studies conducted in India and adjacent country Pakistan [5,10,16]. Endometrial polyps are a benign growth ascertained in 8.6% samples in this study mostly in reproductive and perimenopausal women. One case of hemangiomatic growth in polyp was detected in a 39 yrs female. It was diagnosed 4.1%, 8.95% and 12% in various studies [5,10,16]. Disordered endometrium pattern is usually a hormone induced cystic dilatation pathology common in perimenopausal age because of anovulatory cycle. Higher expression of gene TGFB2 and ligand 18 plays role in its development. Varying size cystic changes were the basis of diagnosis found in 7.61% in this study. In a study it was diagnosed in 32.4% cases as the commonest among functional causes [2]. This was found most common cause of AUB in a study in Tehran [14]. Secretory endometrium is a normal process of menstrual cycle in which endometrial cells prepare for nourishment of ovum. It was diagnosed in 6.6% cases in this study. In different studies it was diagnosed in 2.89% and 11% cases [9,11]. Jetley et al found 32.4% cases as the commonest among functional causes [2].

Endometrial carcinoma commonly involves nulliparous females and hypertension, diabetes, obesity, smoking are the risk factors for its development. Some atypical premalignant condition can also transform into carcinoma. It is more prevalent in western population but in Asia it stands 2nd to cervical carcinoma. Adenocarcinoma is predominant in endometrium but other types like sarcoma and squamous cell carcinoma have also been reported. Malignant polyps were reported in almost one-third cases in a study of Farrell et al [17]. Some rare tumor like malignant mixed mullerian tumor has also been reported [5]. Endometrial carcinoma is most frequent malignant tumor of female reproductive organs in western countries [18]. Three cases of malignancy were diagnosed in this study (1.52%). Papillary variant was seen in 2 cases of 50 yr and 56 yr females, later with complaint of heavy bleeding since five days. It was diagnosed 0.44% in a study [16]. A research diagnosed this in 2.48% patients, and 12.7% in some other study [15,19]. Sometimes cervical carcinoma extends to endometrium and the patient present with bleeding per vaginum [3]. D & C is being replaced by pipelle endometrial biopsy as it is safe, simple operative procedure without compromising accuracy [9].

Conclusion

Abnormal uterine bleeding is a major health problem among females. The inadvertent use of hormonal therapy should be limited and advised only to suitable patients to avoid development of endometrial hyperplasia and disordered proliferative endometrium.

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