A two year histopathological study of endometrial biopsies in a teaching hospital in Northern India

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Abstract

Introduction: Endometrial biopsies and curettings constitute an important tool for diagnosis of endometrial pathology; whether benign, pre-malignant and malignant, and help the gynecologist to decide appropriate therapeutic strategy. The present study was carried out to document the histopathological appearances seen in endometrial biopsies, and their age–wise distribution in patients with infertility and abnormal (irregular, excessive or continuous) uterine bleeding due to endometrial causes.

Materials and Methods: A total of 214 specimens of endometrial curettings and biopsies from patients with abnormal uterine bleeding due to endometrial causes and inability to conceive, received in the Pathology department, Gian Sagar Medical College and Hospital, Banur, Rajpura, over a period of two years from January 2012 upto December 2013, were retrieved and analyzed retrospectively, and their findings were documented. The tissue had been received in 10% formalin, processed routinely, and the slides had been stained with Hematoxylin and Eosin.

Results and Conclusion: The most common histopathological diagnosis was proliferative endometrium seen 33% cases. Products of conception were confirmed histologically in 12% cases. Endometrial hyperplasias were seen in 09% cases, and disordered proliferative endometrium in 06%. Secretory endometrium was seen in 07% cases. 02% biopsies showed atrophic endometrium. Luteal phase defects were seen in 07% of the specimens. 01% cases showed tubercular endometritis and adenocarcinoma each. The most common finding in patients of infertility was proliferative endometrium indicating anovulatory cycles.

Endometrial biopsy is a valuable tool in assessment of endometrial status in infertility, as well as benign and malignant pathology in abnormal uterine bleeding due to relative ease and accessibility of procedure and rapid availability of results.

Keywords: Abnormal uterine bleeding, Infertility, Dysfunctional uterine bleeding, Hyperplasia, Carcinoma.

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Introduction

Abnormal uterine bleeding (AUB) is defined as a pattern of bleeding that does not correspond with the duration, amount and frequency of the flow of a normal menstrual cycle.(1) It is one of the most common problems encountered by gynecologists. The causes of AUB vary with age; in young women in the reproductive age group, it is most commonly due to hormonal imbalance, while in peri-menopausal and post-menopausal women, AUB is generally due to hyperplasias and malignancies.(2)

Histopathological characterization of endometrial biopsies and curettings by the light microscope is considered the gold standard for diagnosis of the etiology of AUB, because of the relative ease and safety of obtaining samples, along with reasonable reporting time and diagnostic accuracy.(3) Endometrial curettings and biopsies exhibit a wide range of histopathological patterns due to normal and abnormal cyclical changes, drugs, hormones, infections and malignancies, thus posing a challenge to practicing pathologists.(4)

Endometrial biopsy is equally important in evaluating patient for infertility. The dating of the endometrium by its histological appearance is helpful clinically to document ovulation, assess hormonal status and determine cause of endometrial bleeding and infertility.(5)

In the present study, 214 samples of endometrial curettings and biopsies received over a period of two years were chosen for retrospective histopathological evaluation of causes of AUB and infertility.

Materials and Methods

This study was conducted in the Department of Pathology, Gian Sagar Medical College and Hospital, Banur, Rajpura, Punjab. 214 specimens of endometrial curettings and biopsies obtained from patients presenting with abnormal uterine bleeding due to endometrial causes and failure to conceive, from January 2012 upto December 2013 were included in the study.

The biopsy specimens had been obtained by conventional dilatation and curettage or biopsy performed as an inpatient procedure. The specimens had been received in 10% formalin and underwent

routine histological processing followed by Hematoxylin and Eosin staining.

A. Criteria for exclusion

1. Patients with organic lesions involving the genital tract like leiomyomas, adenomyosis, cervical and vaginal pathology.
2. Patients with systemic disease like haemostatic disorders etc.

B. **Criteria for adequacy of specimen:** In specimens where no endometrial tissue was seen or no conclusion could be arrived at, in spite of the presence of some tissue, a diagnosis of inadequate for evaluation was given.

Results

The present study included 214 specimens of endometrial curettings and biopsies received in the department over a period of two years; from January 2012 upto December 2013.The patients' ages ranged from 21-65 years, with a mean age of 37.8 years (Table 1). Out of 214 patients, 145 patients presented with abnormal uterine bleeding (AUB). The majority of these patients were in age group of 41-50 years (peri-menopausal).

The most common chief complaint among all patients was menometrorrhagia (irregular and excessive bleeding per vaginum), which was seen in 26% patients, closely followed by menorrhagia (excessive bleeding per vaginum), in 24% cases (Table 2). Presenting complaints were different in different age groups i.e. patients in the 21-30 years age group most commonly presented with an inability to conceive (34%). The most common presenting symptom in women in the age group of 31-40 years and 41-50 years was menometrorrhagia seen in 32% cases, and in 36% cases respectively. Post-menopausal bleeding (54%) was the most common presenting complaint in the age group of 51 years and above (Table 3). After excluding patients of infertility, and complications of pregnancy, the most common chief complaint in the age groups of 20-30 years, 31-40 years, and 41-50 years was menometrorrhagia seen in 58%, 48% and 36% respectively. In the age group of > 50 years, the most common clinical presentation was post-menopausal bleeding.

The most common clinico-radiological diagnosis was dysfunctional uterine bleeding; in 60% patients (Table 4). The most common clinical diagnosis in the age group of 21-30 years was primary infertility (32%), closely followed by dysfunctional uterine bleeding (30%). The latter was also the most common diagnosis in our patients in all the other age groups. 64% patients in the 31-40 years age group, 94% patients in the 41-50 years age group, and 77% patients in the 51 and above age group, were diagnosed as DUB. Malignancy was suspected clinically in two cases only (Table 5). Dysfunctional uterine bleeding was the most common diagnosis in all the age groups of patients exclusive of infertility and complications of pregnancy, and was seen in 88%, 94%, 94% and 77% patients respectively.

The most common histopathological diagnosis among all patients was proliferative endometrium, seen in 33% cases. Products of conception were confirmed histologically in 12% cases. 09% of endometrial samples were designated as inadequate for evaluation. Endometrial hyperplasias were also found in 09% cases. Secretory phase and atrophic endometrium were seen in 07% and 02% of biopsies respectively. 07% biopsies showed luteal phase defects. 01% cases were diagnosed as endometrial adenocarcinoma of the uterus. A single biopsy was diagnosed as tubercular endometritis (Table 6). In addition to the other findings; ciliated metaplasia was noted in 02 cases, and squamous metaplasia was noted in one biopsy.

The most common histopathological diagnosis in the age group of 20-30 years was proliferative endometrium, seen in 38% cases. In the age group of 31-40 years, it was simple hyperplasia without atypia, in 19% of cases. Women from the groups 41-50 years most commonly showed proliferative endometrial in biopsies in 43% cases (mostly taken during bleeding episodes indicating anovulatory cycles). 29% biopsies taken from women in the age group of 51 or more were diagnosed as inadequate for processing and reporting.

After exclusion of patients with infertility, and those presenting with pregnancy related complications, 145 cases of AUB with isolated endometrial pathology remained. Out of these 31% patients showed proliferative endometrium, 13% specimens were inadequate for evaluation, 12% showed simple hyperplasia without atypia, 08% were disordered proliferative endometrium, 07% showed progestin effect, co-ordinated LPD was seen in 05% and dissociated LPD in 3.5% patients, benign endometrial polyps and extensive breakdown were seen in 04% each, atrophy was seen in 3.5% patients, and complex hyperplasia without atypia and adenocarcinoma were seen in 1.5% patients each(Table 6B).

As far as the age wise histopathological diagnosis in patients of AUB is concerned, the most common diagnosis was proliferative endometrium. This was seen in 32% and 43% cases in the 21-30 years and 40-50 years age groups respectively. Simple hyperplasia without atypia was the most common histopathological diagnosis in the 31-40 years age group, in 43% cases. 29% of biopsies from post menopausal women were inadequate for evaluation (Table 6C).

Out of 214 specimens of endometrial biopsies studied, 35 patients presented with complaints of inability to conceive. This included patients with primary (27 patients, 77%) as well as secondary infertility (08 patients, 22.8%). Of these, majority of the patients were in second decade of life (26 patients, 74.2%) (Table 7). Different histological patterns were

seen in these 35 endometrial biopsies performed for infertility including proliferative endometrium (anovulatory) in 66% patients, secretory endometrium (17%), Co-ordinated luteal phase defect (LPD) in 08%, Tubercular endometritis and disordered proliferative endometrium in 03% patients each (Table 8).

Table 1: Age distribution

Age group	Number of patients	Percentage
20- 30 Years	76	36
31-40 Years	59	27
41-50 Years	53	25
>50 Years	26	12
Total	214	100

Table 2: Chief complaints

Chief complaint	Number	Percentage
Metromenorrhagia	56	26
Menorrhagia	51	24
Inability to conceive	35	16
Bleeding per vaginum	34	15
Post-menopausal bleeding	28	12
Metrorrhagia	06	04
Discharge and bleeding per vaginum	03	02
Polymenorrhoea	01	01
Total	214	100

Table 3: Age wise distribution of chief complaints

Chief complaint	20-30 Years		31-40 Years		41-50 Years		>50 Years	
	No.	%	No.	%	No.	%	No.	%
Metromenorrhagia	15	20	19	32	19	36	3	12
Menorrhagia	10	14	18	31	18	34	5	18
Inability to conceive	26	34	09	15	00	00	00	00
Bleeding per vaginum	23	30	11	19	00	00	00	00
Post-menopausal bleeding	00	00	00	00	14	26	14	54
Metrorrhagia	01	01	02	03	02	04	01	04
Discharge and bleeding per vaginum	00	00	00	00	00	00	3	12
Polymenorrhea	01	01	00	00	00	00	00	00
Total	76	100	59	100	53	100	26	100

Table 4: Clinical and radiological diagnosis

Clinical and radiological diagnosis	Number of patients	Percentage
Dysfunctional uterine bleeding	131	60
Incomplete and missed abortion	34	16
Primary infertility	27	13
Secondary infertility	08	04
Endometrial polyp	08	04
Pyometra due to endometrial atrophy	04	02
Malignancy	02	01
Total	214	100

Table 5: Age wise distribution of the clinico-radiological diagnosis

Clinical and radiological diagnosis	20-30 Years		31-40 Years		41-50 Years		>50 Years	
	No.	%	No.	%	No.	%	No.	%
Dysfunctional uterine bleeding	23	30	38	64	50	94	20	77
Incomplete and missed abortion	23	30	11	19	00	00	00	00
Primary infertility	24	32	03	05	00	00	00	00
Secondary infertility	03	04	05	08	00	00	00	00
Benign endometrial polyp	03	04	01	02	03	06	01	04
Pyometra	00	00	00	00	00	00	04	15
Malignancy	00	00	01	02	00	00	01	04
Total	76	100	59	100	53	100	26	100

Table 6 A: Histopathological diagnosis

Histopathological diagnosis	Number of patients	Percentage
Proliferative endometrium	69	33
Products of conception	26	12
Inadequate	20	09
Simple hyperplasia with cystic dilatation without atypia	17	08
Secretory endometrium	16	07
Disordered proliferative	13	06
Progestin effect	11	05
Coordinated LPD	10	05
Benign endometrial polyp	06	03
Extensive breakdown dating not possible	06	03
Atrophic endometrium	05	02
Decidua seen no villi	05	02
Dissociated LPD	05	02
Adenocarcinoma	02	01
Complex hyperplasia without atypia	02	01
Tubercular endometritis	01	01
Total	214	100

Table 6 B: Histopathological diagnosis after excluding patients of infertility and pregnancy related complications

Histopathological diagnosis	Number of patients	Percentage
Proliferative endometrium	43	31
Inadequate	19	13
Simple hyperplasia with cystic dilatation without atypia	17	12
Secretory endometrium	10	06
Disordered proliferative	12	08
Progestin effect	11	07
Coordinated LPD	07	05
Benign endometrial polyp	06	04
Extensive breakdown dating not possible	06	04
Atrophic endometrium	05	3.5
Dissociated LPD	05	3.5
Adenocarcinoma	02	1.5
Complex hyperplasia without atypia	02	1.5
Tubercular endometritis	00	00
Total	145	100

Table 6C: Age wise histopathological diagnosis after excluding patients of infertility and pregnancy related complications

Histopathological diagnosis	20-30 Years		31-40 Years		41-50 Years		51 and over	
	No.	%	No.	%	No.	%	No.	%
Proliferative endometrium	09	32	04	10	23	43	07	27
Inadequate	00	00	02	05	09	17	08	29
Simple hyperplasia without atypia	02	07	11	28.5	04	08	00	00
Secretory endometrium	05	18	04	10	01	02	00	00
Disordered proliferative endometrium	01	3.5	03	08	06	12	02	08
Progestin effect endometrium	01	3.5	05	13	05	10	00	00
Co-ordinated LPD	03	11.5	02	05	01	02	01	04
Benign endometrial polyp	04	14	01	2.5	01	02	00	00
Extensive breakdown	00	00	02	05	01	02	03	11

Atrophic endometrium	00	00	00	00	01	02	04	15
Dissociated LPD	02	07	03	08	00	00	00	00
Adeno carcinoma	00	00	01	2.5	00	00	01	04
Complex hyperplasia without atypia	01	3.5	01	2.5	00	00	00	00
Total	28	100	39	100	52	100	26	100

Table 7: Age group wise distribution of patients of infertility

Age group	Number of patients	Percentage
20-30 Years	26	74
31-40 Years	09	26
41-50 Years	00	00
50 and above	00	00
Total	35	100

Table 8: Histopathological diagnosis in patients of infertility

Histopathological diagnosis	No. of patients	Percentage
Proliferative endometrium	23	66
Secretory endometrium	06	17
Disordered proliferative endometrium	01	03
Progestin effect endometrium	00	00
Coordinated LPD	03	08
Dissociated LPD	00	00
Simple hyperplasia without atypia	00	00
Complex hyperplasia without atypia	00	00
Granulomas	01	03
Inadequate for opinion	01	03
Extensive breakdown	00	00
Total	35	100

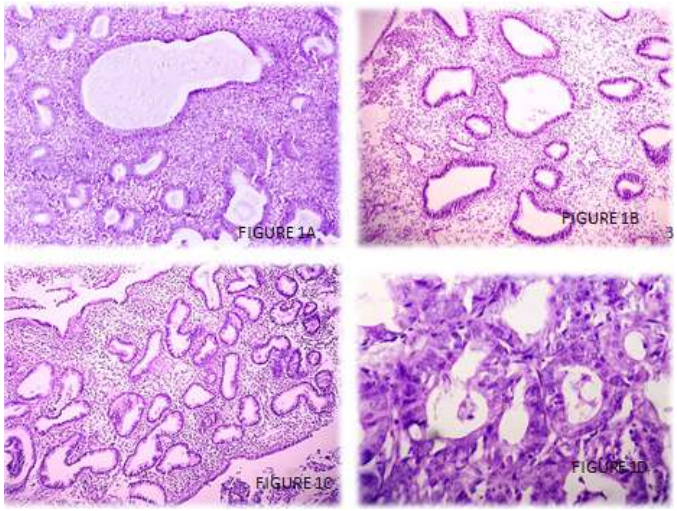

Fig. 1A: Disordered proliferative endometrium, B: Simple hyperplasia without atypia, with cystic dilatation, C: Complex hyperplasia without atypia, D: Endometrioid adenocarcinoma

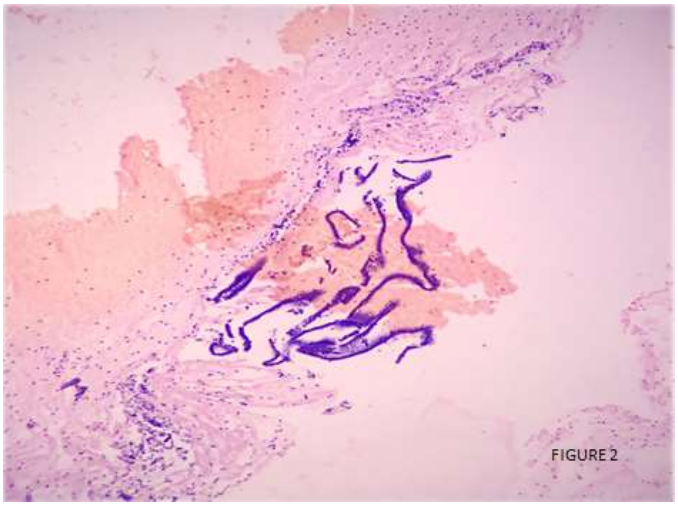

Fig. 2: Atrophic endometrium

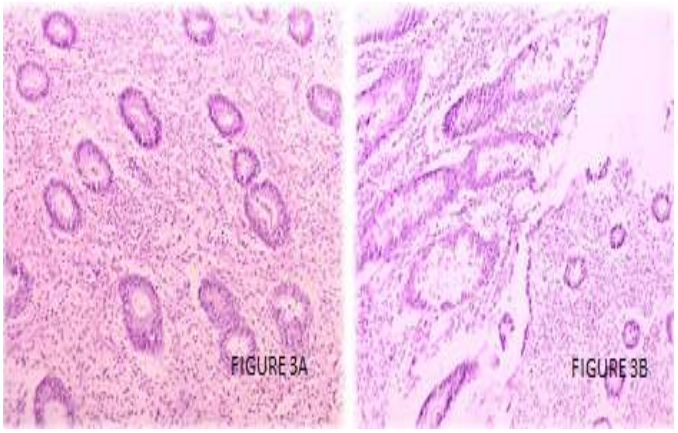

Fig. 3A & 3B: Dissociated luteal phase defect

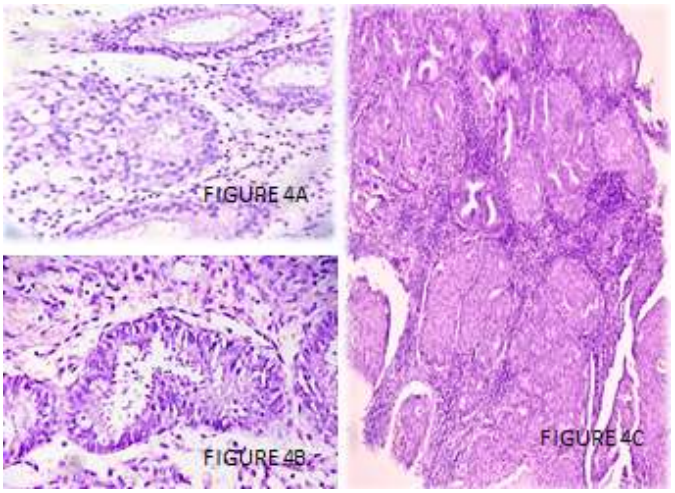

Fig. 4A and B: Ciliated metaplasia, C: Squamous metaplasia

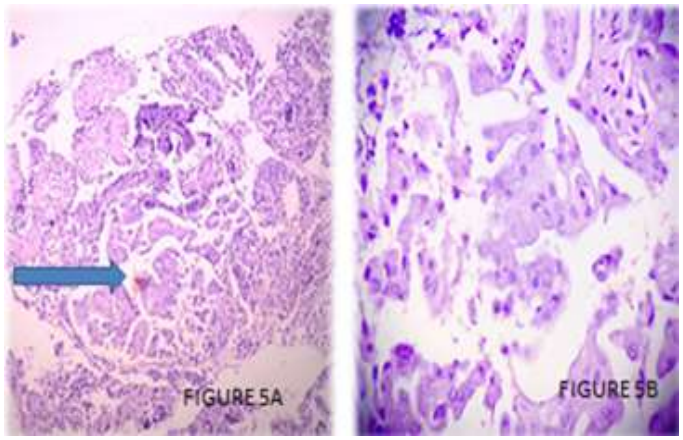

Fig. 5A & 5B: Papillary syncytial metaplasia

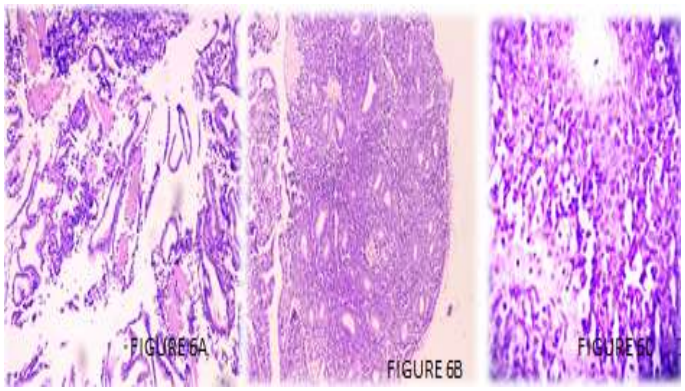

Fig. 6A: Breakdown of glands and stroma, with fibrin thrombi, B: Stromal condensation and glandular crowding in breakdown, C: Foamy macrophages signifying chronic breakdown

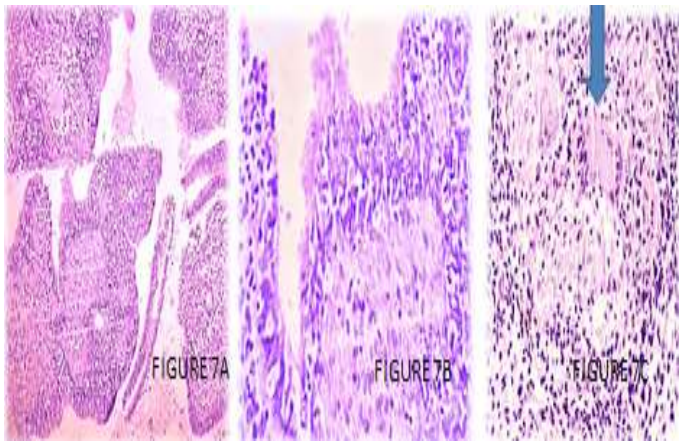

Fig. 7A & 7B: Epithelioid cell granulomas with necrosis, C: Epithelioid cell granuloma with langhans giant cell

Discussion

In most of the cases, endometrial curettage and biopsy are done for evaluation of abnormal uterine bleeding, infertility, or follow up of a previous diagnosis. Interpretation of endometrial biopsy specimens requires a complete and accurate clinical history, menstrual status, and the date of last menstrual period, along with history of exogenous hormones or drugs.[6]

In the present study, 214 specimens of endometrial curettings and biopsies were analysed retrospectively. The ages of the women ranged from 21 to 65 years, with a mean age of 37.8 years. The maximum number of patients (76) belonged to the 20-30 years age group, and around 60% of these women presented either with infertility, or with complications of pregnancy.

After excluding patients presenting with infertility and complications of pregnancy, 145 cases of abnormal

uterine bleeding remained. Among these, the highest percentage of patients (36%) belonged to the 41-50 years (peri-menopausal) age group. Other studies conducted by Yusuf et al (1996), Moghal et al (1997), Saraswati et al (2008) and Mahapatra et al (2015).[7,8,9,10] showed similar results. In these studies, 38%, 40.8% 33.5% and 37.9% patients respectively, belonged to the peri-menopausal age group.

The incidence of AUB is the highest in this age group because of anovulatory cycles. There is proliferation of the endometrium under the influence of estrogen, but in the absence of corpus luteum, and hence progesterone, there is prolonged endometrial stimulation by estrogen, instability of the endometrium, and bleeding.[11]

The most common chief complaint was menometrorrhagia, which was seen in 26% patients, closely followed by menorrhagia, in 24% cases. After exclusion of patients who presented with inability to conceive, or with pregnancy related complications, 145 cases of AUB remained. Among these, the most common presenting complaint was menometrorrhagia in 39% patients, followed by menorrhagia, in 35% patients. Our findings were similar to a study conducted by Devi et al (2015), in which menometrorrhagia was seen in 38% patients, followed by menorrhagia in 34%.

AUB due to uterine causes may present with menorrhagia, menometrorrhagia, polymenorrhea oligomenorrhea or post-menopausal bleeding.**[13]** Studies have shown that organic causes may be found in upto 25% cases of AUB.[14] The rest of the cases where there is no demonstrable organic cause are labelled as dysfunctional uterine bleeding.[15]

Menorrhagia is defined as excessive flow during regular cycles, which may continue for more than 7 days, and involve bleeding of >80 ml/cycle.[16] It is seen in ovulatory DUB. There is no disturbance of the hypothalamic–pituitary-ovarian–axis.[17] The main defect here seems to be a lack of control in the processes of vasoconstriction and haemostasis, which cause dysregulation of the volume of blood lost.[18]

Menometrorrhagia is defined as irregular and heavy bleeding, and occurs in 24% of peri–menopausal women.[19] It generally occurs in anovulatory DUB. Two to three years following menarche, and upto eight years before menopause, anovulatory cycles may occur[20], and cause bleeding as described above.[11]

The occurrence of menometrorrhagia more commonly compared with menorrhagia, as a presenting complaint in the present study could be due to the fact that majority of our patients with AUB had a proliferative endometrium (31%), implying anovulatory cycles.

The most common clinico-radiological diagnosis was dysfunctional uterine bleeding, seen in 131(60%) patients. It was the most common diagnosis in the 31-40 years, 41-50 years, and > 50 years age group categories, seen in 63%, 98% and 77% patients, respectively. However, in the younger patients belonging to the 20- 30 years age group, the most common clinical diagnosis was infertility, seen in 36% patients in this category, followed closely by pregnancy related complications (30%).

Dysfunctional uterine bleeding can occur any time between menarche and menopause, and in both ovulatory and anovulatory cycles.[21] A diagnosis of DUB is one of exclusion[22], and therefore requires a detailed clinical history, physical examination, laboratory and radiological investigations, to rule out any organic pathology.

In anovulatory DUB, bleeding is due to lack of progesterone due to non-development of corpus luteum.[23] Ovulatory DUB includes luteal phase defects and irregular shedding. In the former, the corpus luteum is insufficient, and either it regresses prematurely, or it is unable to produce enough progesterone. The latter is due to persistence of the corpus luteum, leading to progesterone production for a longer period of time.[11]

The ages of the patients clinically diagnosed as DUB in the present study ranged from 23 to 65 years, with a mean age of 40 years. In a similar study by Dadhania et al,[22] the mean age was slightly lower; being 37 years.

The maximum number of patients (40%) belonged to the 41-50 year age group. This finding is in accordance with studies by Yusuf et al, Saraswati et al, Dadhania et al, Bhonsle et al and Muzaffar et al.[7,9,22,24,25] DUB is more commonly seen in the peri-menopausal age group due to occurrence of anovulatory cycles.

Histopathological Diagnosis

1. **Criteria for specimen adequacy and inadequate specimens:** Studies have shown a lot of disagreement among pathologists regarding specimen adequacy.[26] Some authors believe that these specimens should be classified as inadequate only if there is no endometrial tissue, and unassessable, if the tissue is present, but not sufficient to make a diagnosis.[6]

We, on the other hand, labelled our specimens as inadequate, if there was no endometrial tissue, or if no diagnosis could be arrived at, in spite of the presence of biopsy material. Based on the above criteria, a report of inadequate was given in 09% biopsies, which is comparable with other studies by Abdullah et al, and Clark et al. The percentage of inadequate specimens increased with age, and was the highest (29%), in the post-menopausal age group, due to atrophy of the endometrium following lack of estrogen.[11]

2. **Proliferative endometrium:** 31% of our patients presenting with AUB showed proliferative endometrium, in concordance with results obtained by Afghan et al (32.6%), Patil et al (34%) and

Parmar et al (33.3%).[29,30,31] In most of these cases, proliferative endometrium was associated with breakdown, suggesting anovulatory cycles[32].

3. **Disordered proliferative endometrium:** Out of the 214 cases, 06% were diagnosed as disordered proliferative endometrium, and out of the remaining 145 patients with AUB, 08% were assigned a diagnosis of disordered proliferative phase, similar to 8.5% by Abdullah et al, and 10% by Saadia et al.[27,33] Slightly higher percentages (12% and 13%) were seen in studies by Sajitha et al and Vaidya et al.[34,35]

When there is chronic anovulation, ovarian follicles persist for some time and produce estradiol before undergoing atresia, leading to abundant proliferation of endometrium, and mild disorganization of architecture. This produces widespread dilatation of glands, although the gland to stroma ratio remains normal. This is called disordered proliferative endometrium[11].

4. **Secretory endometrium:** 06% of our patients presenting with AUB showed secretory endometrium on histopathology. This percentage is significantly lower than other similar studies by Abdullah et al (24.9%) and Khan et al (13.7%),[27,36] but then the sample sizes in these studies were larger. Moreover, Abdullah et al have not categorized luteal phase defects separately from secretory endometrium. A higher percentage of 30% was reported by Mahapatra et al,[10] but according to the author, this was attributable to the inclusion of cases treated with hormones, for control of bleeding.
5. **Atrophic endometrium:** Atrophy is an important cause of abnormal uterine bleeding in post – menopausal women. The specimen is usually scanty, composed of small strips of endometrium, fragmented glands and few spindled stromal cells. It is important to know that scant tissue does not make the biopsy inadequate, because it represents all that remains of the lining, and hence should be interpreted accordingly.[37] The exact cause of bleeding in atrophy is not known. It is thought that there is injury to superficial thin walled veins because of cystic dilatation of endometrial glands, causing bleeding.[38]

Endometrial atrophy was seen in 02% patients of all the 214 patients included in the study. In similar studies by Saraswati et al, Mahapatra et al, Abdullah et al, Sajitha et al, Vaidya et al and Khan et al,[9,10,27,34,35,36] done on patients with AUB, atrophic endometrium was seen in a comparable 2.4%, 5%, 3.1%, 4.7%, 5.1%, and 3.9%.

6. **Luteal phase abnormalities:** These include luteal phase deficiency and irregular shedding.
   1. Luteal phase deficiency: In LPD, inspite of ovulation, there is insufficient progesterone secretion by the corpus luteum, causing poorly developed secretory change in the endometrium. This leads to a lag in the histological endometrial date. The glands and stroma may also show discordant development.[39] Corpus luteal deficiency was seen in 8.5% of our patients diagnosed as AUB. Different studies have shown variable percentages of Luteal phase deficiencies, ranging from 1.24%[35] to 15.6%.[36]
   2. Irregular shedding: This has been attributed to the persistence of corpus luteum, leading to prolonged secretion of progesterone. A mixed pattern of proliferative and secretory phase is seen at least 5 days after the onset of bleeding.[37] None of our cases showed irregular shedding.
7. **Endometrial epithelial metaplasia:** These are non neoplastic changes involving replacement of endometrial by another different epithelium. They may be focal or diffuse.[40] They may be squamous, mucinous, ciliated, clear cell, hobnail and eosinophilic type. Usually, they involve the non-secretory endometrium and are associated with exogenous hormones, endometrial polyps, pyometra, intra uterine contraceptive devices, endometrial hyperplasias and endometrial carcinomas.[11]

Ciliated cells are common in normal endometrium.[40] So, a diagnosis of ciliated metaplasia should be reserved only for cases having extensive ciliation, and abundant eosinophilic cytoplasm like that of the fallopian tube.[6]

Squamous metaplasia is usually focal, but when it is widespread, it may obliterate the glandular lumina. It may be typical, or morular type, and may be associated with presence of polyps, hyperplasia and endometrial carcinoma.

Papillary syncytial metaplasia is a misnomer, as it actually denotes repair associated with endometrial breakdown. In this, there is formation of syncytia of endometrial epithelial cells having eosinophilic cytoplasm, and lacking stromal support. It needs to be differentiated from serous papillary adenocarcinomas.[11]

Two of our cases showed ciliated metaplasia, one showed squamous metaplasia of the morular type, while papillary syncytial metaplasia was also seen in one case.

8. **Endometrial polyps:** Endometrial polyps have been reported in 2-23% patients presenting with abnormal uterine bleeding in both premenopausal and post-menopausal women. If the gynecologist knows of the presence of a polyp, it is removed intact, and the diagnosis is easy. If however, the presence of a polyp is not being suspected, its fragments are usually received admixed with the rest of the endometrium in the biopsy. In such a situation, clues to the diagnosis are the polypoidal shape, the fibrous stroma with thick walled vessels

and different glandular architecture (focal dilatation and crowding).[6]

Endometrial polyps were seen in 04% of our patients. In similar studies by Mahapatra et al, Sajitha et al, and Khan et al,[10,34,36] endometrial polyps were seen in 3.6%, 5.12%, and 3.9% patients, which is comparable to the findings in present study.

9. **Effects of exogenous hormones and drugs:** Progestin only compounds are administered for abnormal uterine bleeding, and suppress ovulation, consequently inhibiting endometrial growth. There is glandular atrophy, with pseudo- decidualization of the stroma. An inflammatory infiltrate composed of lymphocytes may be seen. High dose therapy may cause marked proliferation, and a lot of polypoidal tissue is obtained at biopsy. Breakdown change may be present.[11] Progestin effect was seen in the endometrium in 07% of our patients.
10. **Break down changes in menstrual endometrium, and in dysfunctional uterine bleeding:** The morphological features of breakdown include glandular changes like accumulation of apoptotic debris, in the basal cytoplasm of the glands and papillary syncytial metaplasia. Stromal changes include collapse, followed by aggregation into tight clusters, known as stromal blue balls. Fibrin thrombi are seen in blood vessels. Evidence of chronic bleeding includes accumulation of hemosiderin within stroma, or within macrophages, and presence of foam cells. The difference between menstrual breakdown and the breakdown in dysfunctional uterine bleeding is that in the former, secretory changes are present in the glands, the process is diffuse, and there are no features of chronic bleeding.[37] Breakdown was seen in all 145 cases of AUB, in whom biopsy was taken during the bleed**.**
11. **Endometrial hyperplasia:** According to 1994 WHO classification, endometrial hyperplasias are divided into simple and complex forms depending on the glandular architecture. In simple hyperplasia, the normal gland to stroma ratio is largely maintained, although there may be a slight increase. In complex hyperplasia, there is an increase in the gland to stroma ratio. Simple and complex hyperplasias are further divided into atypical and non-atypical categories on the basis of presence or absence of nuclear atypia. [6]

In the present study, out of 145 patients who presented with abnormal uterine bleeding, endometrial hyperplasia was seen in 19 patients (13%), which was second common diagnosis after proliferative endometrium in this category. Of these, 17(12%) patients had simple cystic hyperplasia without atypia and 02(1.3%) patients had complex hyperplasia without atypia.

A comparable sample size of 219 cases was studied by Jetley et al,[41] who reported 24 patients with endometrial hyperplasia (10.9%). Similar incidence of endometrial hyperplasia has been reported by Dangal et al and Slobada et al.[42,43] Identification of endometrial hyperplasia is important as it is thought to be precursor of endometrial carcinoma.[36]

12. **Endometrial carcinoma:** This is the most common carcinoma of the female genital tract.[44] The common etiological factors include exogenous hormones (estrogens)[45], obesity[46] and decreased physical exercise[47]. Early age at first pregnancy confers a protective effect.[48] The endometrioid subtype of carcinoma is the most common form encountered.[49]

In the present study, two cases (01%) were diagnosed as endometrial carcinoma, and both were of the endometrioid subtype. Similar low incidences have been obtained in studies by Saraswati et al (02%), Mahapatra et al (0.7%), Dadhania et al (2.6%), Abdullah et al (1.8%), Vaidya et al (2.4%) and Baral et al (1%).[9,10,22,27,35,38] All these studies have Asian women as subjects, and reflect and overall lower incidence of endometrial carcinoma in the east, compared with the west due to early childbearing, lesser obesity and a more active life style compared with the west.

13. **Artifacts in endometrial biopsies:** Identification of artifacts is important because these may be confused with hyperplasia or carcinoma. These include telescoping, which is a gland in gland appearance, and is due to mechanical disruption of these glands. Also included is artifactual crowding of glands, which may mimic a hyperplasia. The tearing of the surrounding tissue helps differentiate it from hyperplasia. Another artifact is pseudo-papillary endometrium, wherein the biopsy shows only strips of epithelium, forming papillae like structures, causing confusion with benign and malignant papillary lesions of the endometrium.[11]

Infertility

Infertility is defined as inability of a couple to achieve conception after one year of unprotected coitus. In female partner, this is accounted for largely by disturbance of menstrual cycle, which leads to infertility by changing the histologic appearance of endometrium due to which blastocyst fails to implant and this leads to infertility.[50] Endometrial biopsy is done to determine cause of primary and secondary infertility by endometrial patterns and to assess importance of luteal phase defect in infertility.

Out of 214 endometrial biopsies studied, 35 were performed on patients who presented with complaints of inability to conceive. This included 27 patients with primary infertility, and 08 patients with secondary infertility. Of these, majority of the patients (26 patients, 74.2%) were in second decade of life,

reflecting an early age of marriage in our cohort of patients.

Different histological patterns were seen in the 35 endometrial biopsies performed on patients with complaint of infertility which included secretory endometrium(17%), proliferative endometrium (anovulatory) in 66% patients, Co-ordinated luteal phase defect (LPD) in 08%, Tubercular endometritis and Disordered proliferative endometrium in 03% patients each.

Other studies with similar categorization of histological diagnosis have been done on different number of endometrial biopsies in infertility.[51,52,53] The higher percentage of secretory endometrium in the above mentioned studies could be due to the fact that in these studies secretory endometrium and luteal phase defects have been clubbed together.

In present study, tuberculous endometritis was seen only in one patient (3%) in concordance with Punyashetty et al[53] who reported 3.9% cases. Tubercular endometritis is a major problem in developing countries, and idiopathic cases should be investigated for tuberculosis.

Conclusion

Endometrial biopsy is an important tool to diagnose gynecological conditions in patients. It not only shows the hormonal response of endometrium, but gives additional information about the local factors of endometrium concerning atrophy, specific and non-specific infections and malignancy[54]. It is a reliable yardstick to measure incidence of these conditions which lead to infertility or abnormal uterine bleeding in females[5].

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