International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2020; 3(1): 88-91
Received: 11-11-2019
Accepted: 15-12-2019

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Study of spectrum of endometrial pathology in patients with abnormal uterine bleeding and its clinicopathological correlation

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DOI: https://doi.org/10.33545/pathol.2020.v3.i1b.158

Abstract
Background: The term abnormal uterine bleeding (AUB) is defined as any bleeding from uterus not fulfilling the criteria of normal uterine bleeding in terms of frequency, duration and amount. AUB is one of the most common complaints in gynaecological OPDs resulting in endometrial sampling.
Material and methods: The present study was conducted in SHKM Government Medical College Nalhar, Nuh, Haryana from January 2018 to November 2019 by Departments of Pathology and Gynaecology. One hundred eighty cases of AUB were included in the study.
Endometrial samples such as endometrial biopsy, dilatation and curettage material (D&C), fractional curettage specimens and hysterectomy specimens were included in the study. Gross and microscopic features were studied.
Results: The age group of patients in this study ranged from 20 to 67 years. Maximum numbers of cases (n=90) were in the age group of 40 to 49 years. Most common presenting complaint was menorrhagia (50.5%). Normal cyclical endometrium was found to be the commonest histopathological pattern with proliferative endometrium in 48.8% and secretory endometrium in 22.2% cases. On histopathology rest of the cases revealed disordered proliferative phase in 20(11.1%) cases, endometrial hyperplasia in 2(1.1%), chronic endometritis in 8(4.4%), granulomatous inflammation in 2(0.01%), senile cystic atrophy in 6(3.3%) and malignancy in 4(2.2%) cases.
Conclusion: Disordered proliferative phase endometrium, hyperplasia and carcinoma endometrium are seen more commonly in perimenopausal and postmenopausal females. Hence, histopathological 3 examination should be considered mandatory in women above 40 years of age presenting with AUB to rule out any malignant pathology.

Keywords: Abnormal uterine bleeding, endometrium, histopathology

Introduction
Endometrium is a hormonally sensitive tissue which undergoes cyclic changes during reproductive period. The term abnormal uterine bleeding (AUB) is defined as any bleeding from uterus not fulfilling the criteria of normal uterine bleeding in terms of frequency, duration and amount. When AUB occurs during reproductive years and is not associated with a detectable uterine abnormality other than nonsecretory patterns and excluding atypical hyperplasia and carcinoma, it is called dysfunctional uterine bleeding (DUB) [1, 2]. AUB is one of the most common complaints in gynaecological OPDs resulting in endometrial sampling. The social and economic cost of menorrhagia is considerable [1, 3]. The histopathology of endometrial samples is one of the major diagnostic tools in the workup of patients with AUB. The present study was carried out to evaluate AUB in various age groups, to study histopathology of the endometrium in cases of AUB and to analyse the clinicopathlogical patterns.

Material and Methods
The present study was conducted in SHKM Government Medical College Nalhar, Nuh, and Haryana from January 2018 to November 2019 by Departments of Pathology and Gynaecology. One hundred eighty cases of AUB were included in the study. Detailed clinical history including age, pattern and duration of abnormal bleeding, menstrual history, obstetrics history, past history, physical examination, pelvic examination and laboratory as

well as imaging investigations were recorded. Patients on hormonal therapy, patients with intrauterine contraceptive device, pregnant females with history of bleeding, isolated cervical and vaginal pathology, leiomyoma, bleeding due to previously diagnosed gynaecological malignancy, homeostatic disorders and autolysed specimens were excluded from the study. The functional causes of AUB included in this study were normal cyclic phases of the endometrium and other abnormal physiological changes in the endometrium (atrophic endometrium, disordered proliferative endometrium). Organic lesions which were included as the cause of AUB in this study include chronic endometritis, hyperplasia and endometrial carcinoma.

Endometrial samples such as endometrial biopsy, dilatation and curettage material (D&C), and fractional curettage specimens were fixed in 10% formalin and processed in histopathology laboratory. After detailed gross examination, whole of the tissue was embedded, paraffin blocks of the tissue were made, and sections were cut and stained with hematoxylin and eosin. The data collected for the study was statistically analysed.

Results

The age of the patients ranged from 20 to 67 years in this study. The patients were categorised into 6 age groups. Maximum number of patients (n=90) were in the age group of40-49years followed by 36 cases in the age group of 30-39 years. Least number of patients were in the group 50-59 years (n=12). [Table-1]

The patients presented with complaints ranging from Oligomenorrhoea to menorrhagia. Maximum number of patients presented with menorrhagia (50.5%), followed by polymerrrhoea (18.9%), oligomenorrhea (10%), menometrorrhagia (7.8%), metrorrhagia (5.6%). Five percent patients presented with continuous bleeding per vaginum and 2.2% presented with postmenopausal bleeding. [Table-2]

We also studied if there was any correlation of AUB with parity. Nulliparous females constituted 15.6% of cases. Maximum number of cases were multiparous with para 3 and para 4 women and comprised 35.6% cases. Grand multipara i.e para 5 and more comprised 32.8% cases. Para 1 and 2 patients were 16.4% in this study.

Histopathological examination revealed proliferative phase endometrium in 88(48.8%), secretory phase endometrium in 40(22.2%), disordered proliferative phase 20(11.1%) [Figure-1], endometrial 6hyperplasia 2(1.1%) [Figure-2], chronic endometritis 8(4.4%), granulomatous inflammation 2(0.01%), senile cystic atrophy 6(3.3%) and malignancy in 4(2.2%) [Figure-3] cases. Four samples were inadequate and comprised of blood clot only. [Table3 &4]

Table 1: Agewise distribution of cases of AUB

Age Group	Number of Patients	Percentage
10-19	0	0
20-29	28	15.5%
30-39	36	20%
40-49	90	50%
50-59	12	6.6%
>59	14	7.7%
Total	180	

Table 2: Distribution of cases according to clinical presentation

Clinical symptoms	Number	Percentage
Menorrhagia	91	50.5%
Polymenorrhoea	34	18.9%
Metrorrhagia	10	5.6%
Menometrorhagia	14	7.8%
Oligomenorrhoea	18	10%
Continuous bleeding	9	5%
Postmenopausal bleeding	4	2.2%
Total	180	

Table 3: Histopathological pattern of endometrium

Histopathology	Number	Percentage
Proliferative phase	88	48.8%
Secretory phase	40	22.2%
Disordered Proliferative Phase	20	11.1%
Hyperplasia	8	4.4%
Endometritis	8	4.4%
Granulomatous inflammation	2	1.1%
Malignancy	4	2.2%
Atrophic Endometrium	6	3.3%
Inadequate	4	2.2%
Total	180	

Table 4: Correlation of histopathological findings with age group

Histopathology	10-19	20-29	30-39	40-49	50-59	>59	Total
Proliferative phase		16	24	42		6	88
Secretory phase		6	10	16	8	-	40
Disordered Proliferative Phase		-	-	20	-	-	20
Hyperplasia		-	-	8	-	-	8
Endometritis		4	-	4	-	-	8
Granulomatous inflammation		2	-	-	-	-	2
Malignancy		-	-	-	-	4	4
Atrophic Endometrium		-	-	-	2	4	6
Inadequate		-	2	-	2		4
Total		28	36	90	12	14	180

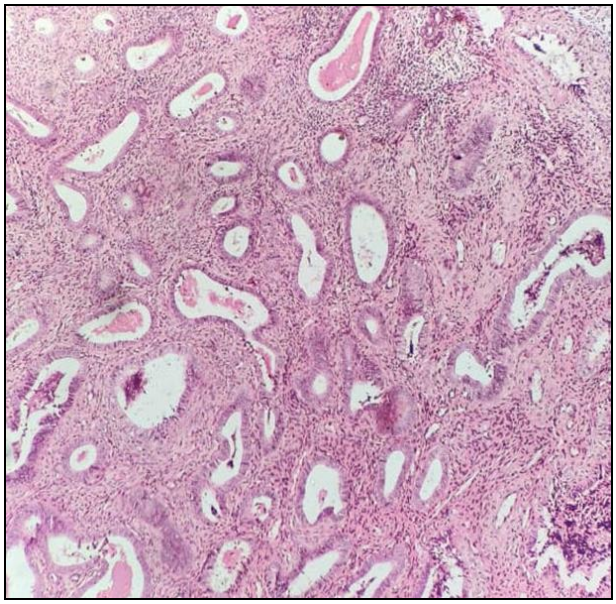

Fig 1: Photomicrograph showing endometrium in disordered proliferative phase [H&E X200]

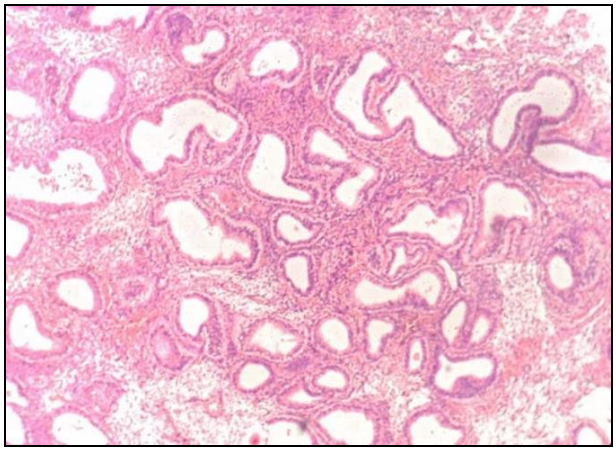

Fig 2: Photomicrograph showing non atypical hyperplastic endometrium [H&EX200]

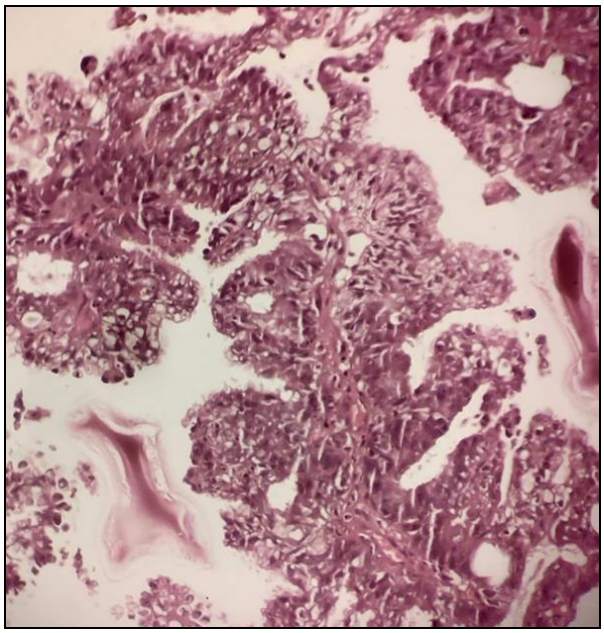

Fig 3: Photomicrograph showing adenocarcinoma endometrium [H&E x200]

Discussion

Etiology of AUB varies according to age as to whether the patient is premenopausal, perimenopausal or postmenopausal. Various studies suggest that AUB occurs most often at extremes of reproductive age, a time when anovulation is frequent. Endometrial curettage followed by histopathological examination is an important diagnostic and therapeutic tool especially in perimenopausal and postmenopausal age groups [4].

Our patients ranged from 20-67 years of age. Maximum patients were in the age group of 40-49 years (50%) closely followed by 20% patients in 30-39 years. This is in concurrence with the other studies. Gleeson *et al*. [5] reported 28-49 years as the most common age group. Similar observations were also made by Bindroo S *et al*. [1], Bolde *et al*. [2], Vaidya *et al*. [5] and Jairajpuri *et al*. [6].

Increased number of cases in this perimenopausal age group may be due to decrease in number of Graafian follicles resulting in low level of estrogen which cannot maintain the normal growth of endometrium [1].

Uterine bleeding interferes with the quality of life in otherwise healthy women. Symptoms vary from Oligomenorrhoea to menorrhagia. Menorrhagia is bleeding occurring at normal intervals (21-35 days) but with heavy flow (>80ml) or duration (>7days). Metrorrhagia is bleeding of any amount which is a-cyclical and which occurs irregularly or continuously in between normal cycles. Menometrorrhagia is bleeding occurring at irregular, noncyclic intervals and with heavy flow. Polymenorrhoea is bleeding which occurs at frequent intervals of less than 21 days but which is normal in amount. Oligomenorrhoea is bleeding occurring at intervals greater than 35 days. Postmenopausal bleeding is bleeding occurring in a menopausal woman at least one year after cessation of cycles [4].

In the present study, on analysing the patients according to bleeding pattern, the most common presenting complaint was menorrhagia (50.8%) followed by polymernorrhoea (18.9%). Towbin NA *et al*. [7] and Muzzafar M *et al*. [8] also reported menorrhagia as the most common complaint in their studies.

On correlating parity of patients with AUB, it was found that the incidence of AUB is more in multiparous women with para 3 and more. Similar results were reported by Rehana *et al*. [3]. However, there is some discordance in the incidence of AUB in grand multiparous women. In our study, 32.8% patients who suffered with AUB were grand multiparous whereas Rehana *et al*. reported 20.8% cases. This may be due to the fact that there is high incidence of grand multipara in the population in our study group because of low literacy rate in this area.

Histopathological evaluation revealed proliferative phase endometrium in 48.8% cases and secretory phase endometrium in 22.2% cases. Muzzafar *et al*. [8] and Fakhar S *et al*. [9] also reported proliferative phase in 46.6% and 54% cases respectively. Rehana *et al*. reported proliferative endometrium in 6.8% cases only. Secretory phase endometrium has been reported in other studies as 30.8% and 35.4% [10, 8].

Disordered proliferative phase was seen in 11.1%, endometrial hyperplasia in 4.4% and malignancy in 2.2% cases. Disordered proliferative endometrium resembles simple hyperplasia but the process is focal rather than

diffuse [1].

All the cases of disordered proliferative phase endometrium and hyperplasias were in the age group of 40-49 years and all the four cases of malignancy in >59 years' age group. Identification of focal and diffuse endometrial hyperplasia is important as it is thought to be a precursor of endometrial carcinoma. Reed SD *et al.* also reported endometrial hyperplasia peak in perimenopausal and postmenopausal group [11].

Risk factors for endometrial hyperplasia and adenocarcinoma are obesity, hypertension, diabetes and exogenous hormones. Abnormal uterine bleeding in peri and postmenopausal group requires proper evaluation and follow up to confirm or rule out the possibility of malignancy [3].

Chronic endometritis and granulomatous endometritis were seen in 4.4% and 1.1% cases respectively. Four out of total 8 cases of chronic endometritis, and all the cases of granulomatous endometritis (n=2) were in the age group of 20-29 years.

Predisposing factors for chronic endometritis include intrauterine contraceptive device insertion, after pregnancy and abortion which may be due to viral, Chlamydial or Gonoccocal infections. Infertility is the most common complaint seen in patients with granulomatous endometritis [3].

Conclusion

Analysis of histopathology in patients of AUB across the study groups revealed the following:

Patients in the reproductive age group must be carefully screened for infectious causes. Early diagnosis of infectious conditions is important because with treatment, endometrium can be restored to normalcy.

Disordered proliferative phase endometrium, hyperplasia and carcinoma endometrium are seen more commonly in perimenopausal and postmenopausal females. Hence, it is imperative to rule out any malignant pathology in women above 40 years of age presenting with AUB.

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