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Original Research Article

Histopathological Study of Endometrium in Abnormal Uterine Bleeding

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Conflict of interest: Nil

Abstract:

Background: Abnormal uterine bleeding (AUB) may be defined as a bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause.[1] AUB is the commonest presenting symptom in gynaecology out-patient department which has significant morbidity. Endometrial sampling is a first diagnostic step in AUB, but its interpretation is quite challenging to the pathologist.

Methods: This is a hospital based observational study for a period two years in the department of pathology, Andhra medical college from June 2018 to May 2020 with a sample size of 470 cases.

Results: A total of 470 cases with a provisional diagnosis of AUB were studied. The present study includes patients in the age range of 16-66 years with mean age of 41.2 years. The maximum incidence of AUB was in peri -menopausal age (41-50years) and the most common presenting symptom was menorrhagia (62.97%). Majority of patient show normal cyclical endometrium (52%) and only few cases show a definite endometrial pathology. Among the organic lesions endometrial hyperplasia was the common finding(12.97%) which was more common in perimenopausal age.

Conclusion: Abnormal uterine bleeding (AUB) is the commonest presenting symptom in women attending to gynecology department. Endometrial sampling could be effectively used as diagnostic step in AUB, to evaluate the causes of AUB in different age groups and helpful for the detection of hyperplasias and guides the physician in treatment.

Keywords: Endometrium, Abnormal Uterine Bleeding, Menorrhagia.

Introduction

Abnormal uterine bleeding (AUB) may be defined as bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause. It is estimated that 30% of women of reproductive age suffer from menorrhagia. The prevalence increases with age, peaking just prior to menopause. Most cases are associated with anovulatory cycles, in adolescent and perimenopausal women, whereas organic pathologies like hyperplasias and carcinomas are common in post-menopausal group.

Aims and Objectives:

The aims and objectives of this study are to

1. Analyse the histomorphological patterns of endometrium in patients presenting with abnormal uterine bleeding.
2. Estimate the incidence of AUB in various age groups.
3. To correlate present study with the results of other studies.

Materials and Methods:

The present study is a two year observational study in the department of pathology, Andhra medical college from June 2018 to May 2020. Relevant clinical data, lab investigation results, and sonological and hysteroscopic findings were recorded in a structured proforma. All the specimens were fixed in 10% formalin, routinely processed and paraffin embedded tissue sections were made, stained with hematoxylin and eosin stain. Data analysis was done in the form of percentages and proportions and represented as tables and figures.

Inclusion Criteria:

All the patients with a provisional diagnosis of AUB and who underwent Dilatation and curettage (D&C) or hysterectomy were included in the study.

Exclusion Criteria:

Patients with leiomyomas, cervical or vaginal pathology, hemostatic disorders, were excluded

Results: A total of 470 patients with a clinical diagnosis of AUB were studied. Among these 293 were D&C samples and 177 were total hysterectomy samples

Age Distribution:

The present study includes patients with AUB in the range of 16 to 66 years.

AUB is more common in perimenopausal and late reproductive age group with 41-50 years (199 cases) followed by 31-40 years (167 cases).

Table 1: Showing Age Distribution

Age	No. of patients	Percentage (%)
<20	7	1.48
21-30	49	10.42
31-40	167	35.53
41-50	199	42.34
51-60	44	9.36
>60	4	0.85

Parity: The present study includes patients from nullipara to grand multipara where the bulk of patients affected were of para 2 (81%) followed by para 3(10%).

Table 2: Parity

Parity	No. of patients	Percentage (%)
0	9	1.91
1	10	2.10
2	385	81.91
3	47	10
4	14	2.97
5	5	1.06

Pattern Of Bleeding: The predominant pattern of bleeding in this study was menorrhagia (62.97%) followed by metrorrhagia(23.4%) and postmenopausal bleeding (11.27%)

Table 3: Showing Pattern of Bleeding

Pattern of bleeding	No. of patients	percentage
Menorrhagia	296	62.97
Metrorrhagia	110	23.4
Polymenorrhoea	11	2.34
Postmenopausal	53	11.27

Histopathological Pattern Of Endometrium: In the present study out of 470 endometrial samples presenting with abnormal uterine bleeding, major bulk 272 (58%) cases revealed normal cyclical endometrium (proliferative and secretory phase of endometrium) and a smaller group of cases 198 (42%) showed definitive endometrial pathology. Among the organic lesions endometrial hyperplasia account for most of the cases (12.97%).

Table 4: Showing Histopathological Pattern of Endometrium:

Sl.No.	Histopathological Pattern of endometrium	No. of cases	Percentage (%)
1	Proliferative phase	172	36.59
2	Secretory phase	100	21.27
3	Disordered proliferative endometrium	7	1.48
4	Irregular ripening	7	1.48
5	Irregular shedding	5	1.06
6	Pill endometrium	12	2.55
7	Atrophic endometrium	31	6.59

8	Pregnancy related	15	3.19
9	endometritis	6	0.85
10	metaplasias	6	1.70
11	Endometrial polyps	29	6.16
12	Endometrial hyperplasias	61	12.97
13	Endometrial carcinomas	3	0.85
14	Endometrial stromal sarcomas	1	0.21
15	inadequate	14	2.97
16	total	470	100

Table 5: Histopathological Patterns of Endometrium in Different Age Groups:

Endometrial pattern	**Age (Years)**						
	<20	**21-30**	**31-40**	**41-50**	**51- 60**	**>60**	**Total**
Proliferative phase	0	20	70	76	6	0	172
Secretory phase	0	12	49	38	1	0	100
Disordered proliferative	0	1	3	3	0	0	7
Luteal phase defect	0	0	6	6	0	0	12
Pill endometrium	0	2	4	5	1	0	12
Atrophic endometrium	0	0	1	11	15	4	31
Pregnancy related	6	7	2	0	0	0	15
Endometritis	1	2	3	0	0	0	6
Metaplasias	0	0	1	2	3	0	6
Endometrial polyps	0	0	7	20	2	0	29
Endometrial hyperplasia	0	4	17	32	8	0	61
Endometrial carcinoma	0	0	0	2	2	0	4
Endometrial stromal sarcoma	0	0	0	1	0	0	1
Inadequate	0	1	4	3	6	0	14
Total	7	49	167	199	44	4	470

Photographs:

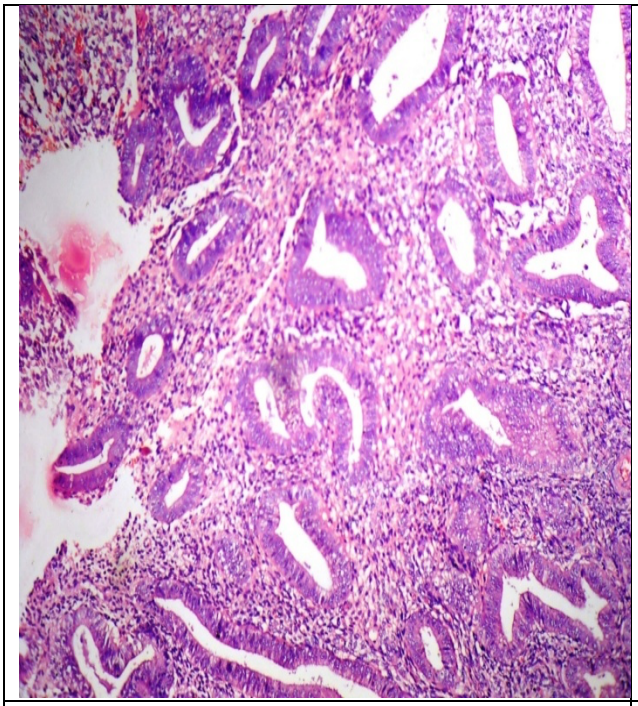

Figure 1: Late proliferative endometrium H&E(40x) showing short and straight tubular glands and compact stroma

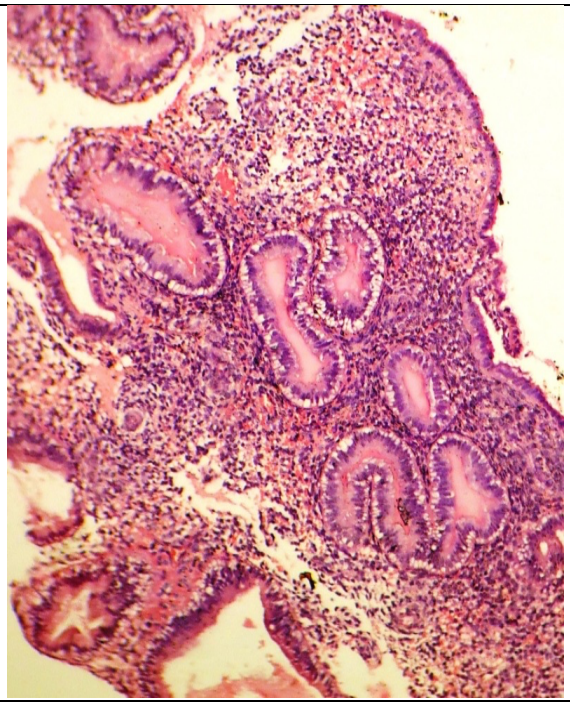

Figure 2: Early secretory endometrium H&E(40x) showing endometrial glands with subnuclear vacuolation

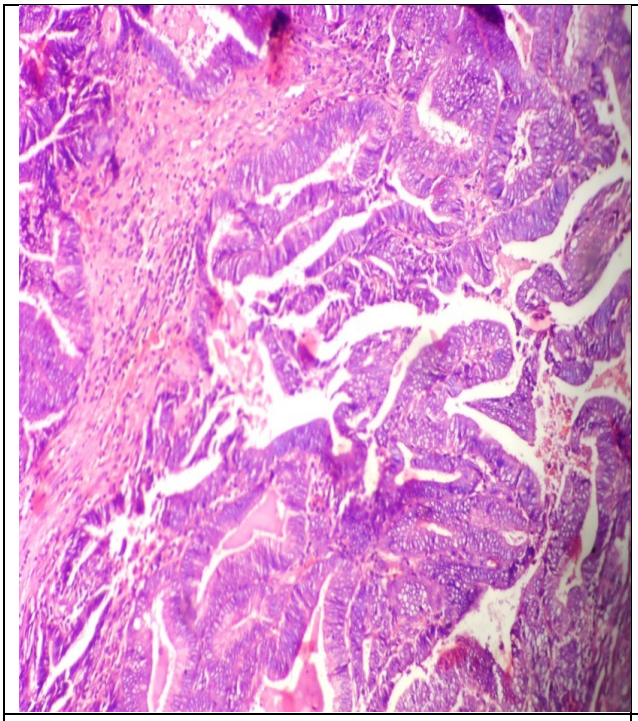

Figure 3: Non atypical hyperplasia H&E(40x) showing crowded glands with complex architecture and scanty stroma.

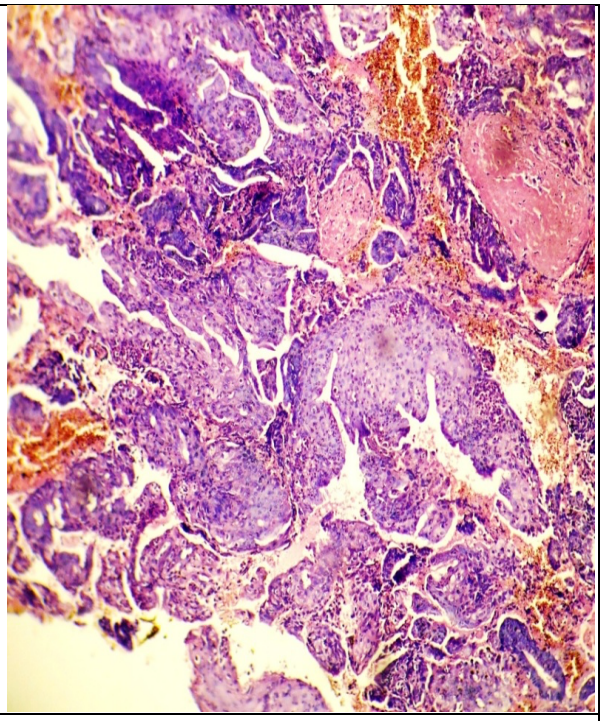

Figure 4: Squamous metaplasia H&E(40x) showing showing endometrial glands with squamous metaplasia

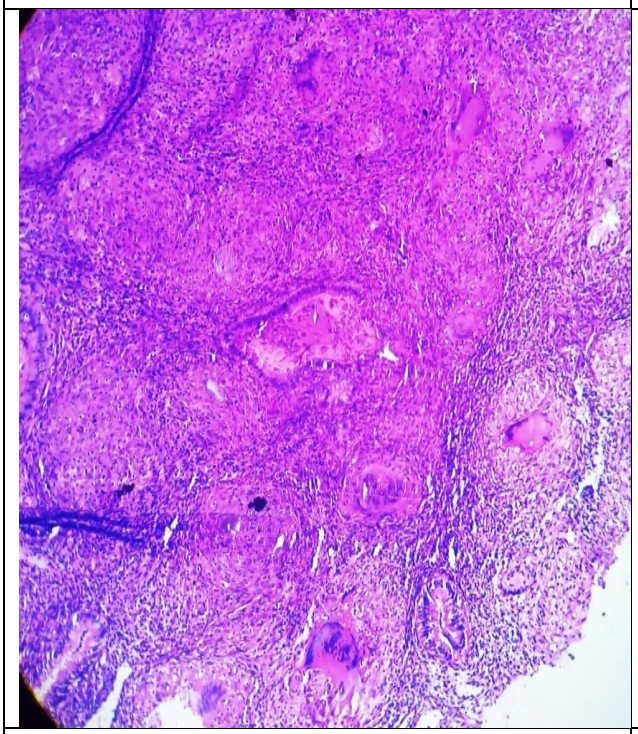

Figure 5: Tuberculous endometritis H&E(40x) showing epithelioid granulomas with Langhans giant cells within the endometrium.

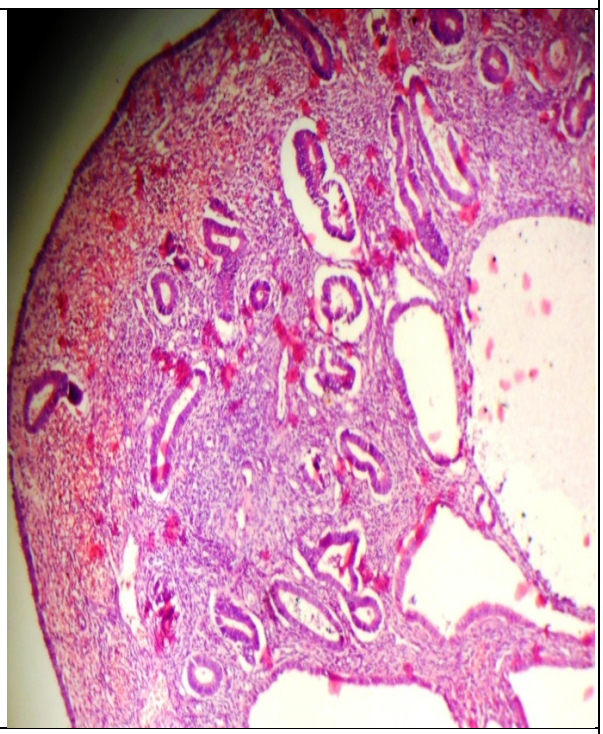

Figure 6: endometrial polyp microscopy H&E(40x) showing endometrial glands, cystically dilated glands and thickened blood vessels.

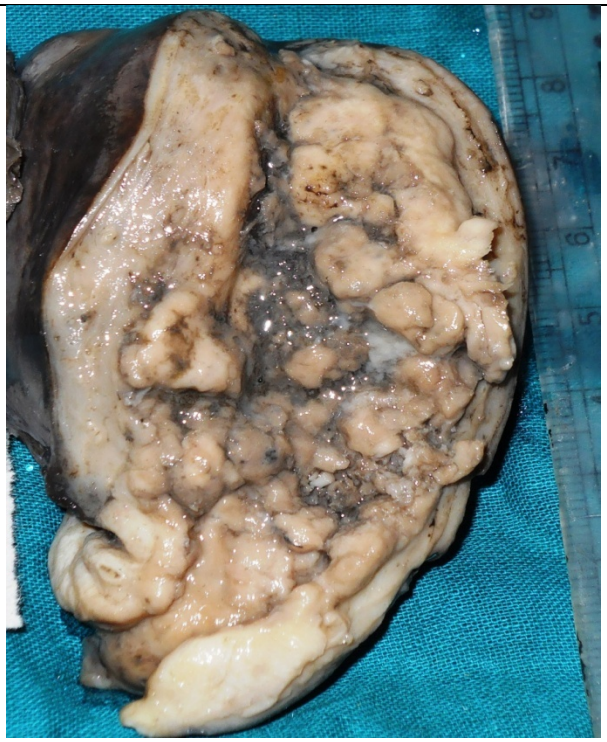

Figure 7: Endometrial carcinoma - Gross Showing an ulcerative and polypoidal growth within the endometrial cavity.

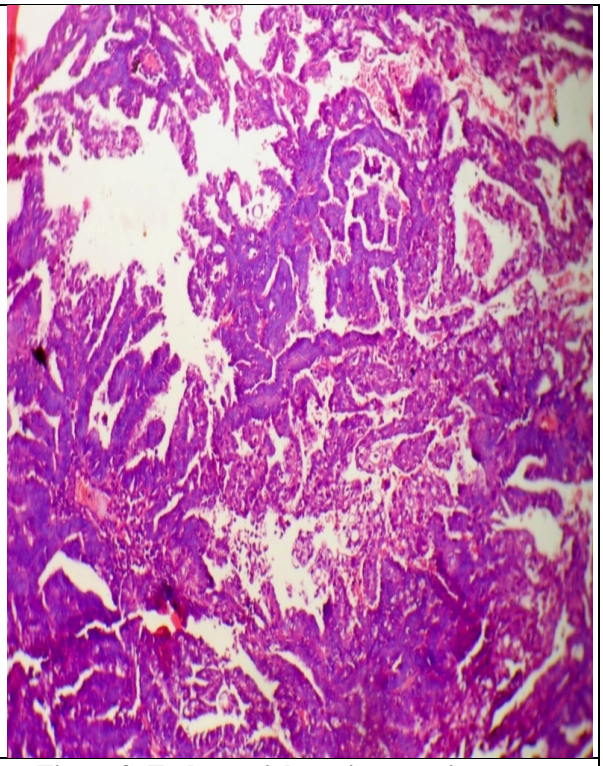

Figure 8: Endometrial carcinoma microscopy H&E(10x) showing complex glandular arrangement with back-to-back arrangement of glands and stromal invasion.

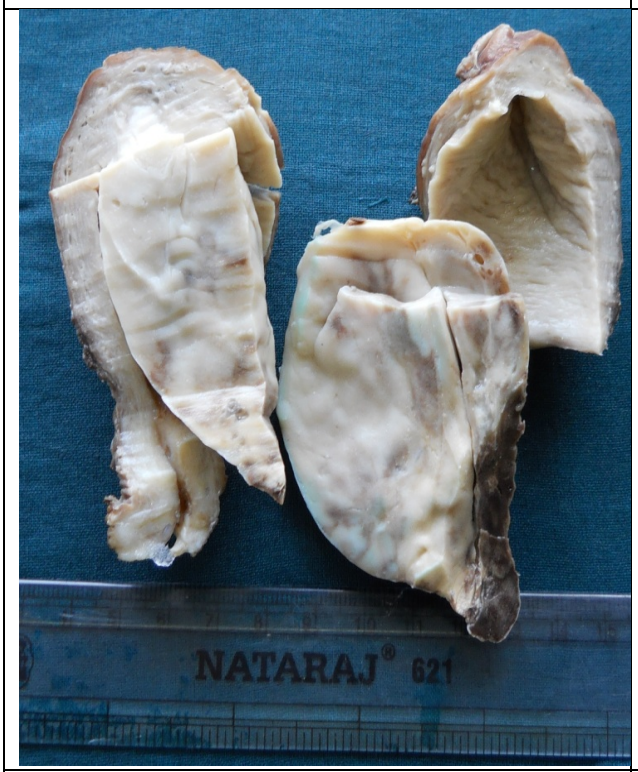

Figure 9: endometrial stromal sarcoma Gross showing fleshy growth in endometrial cavity

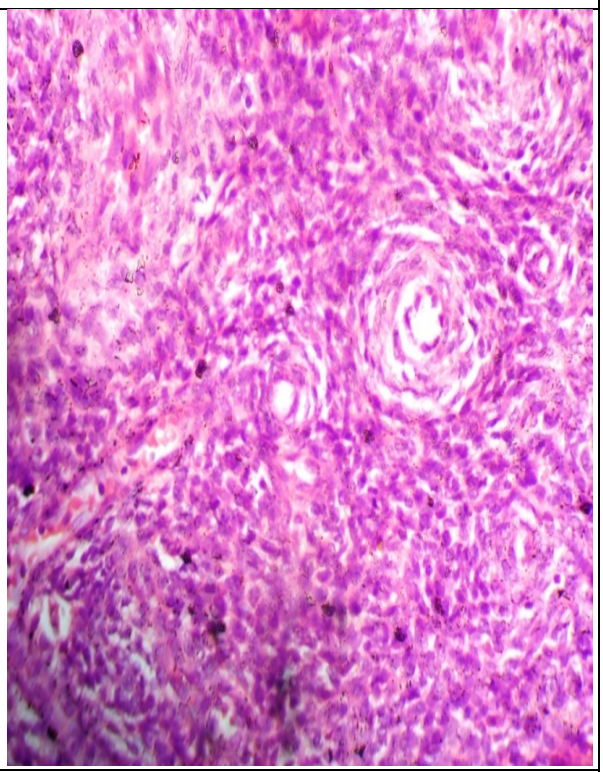

Figure 10: endometrial stromal sarcoma H&E(40x) showing plump spindle cells and mitosis

Discussion

In the present study a total of 470 cases with a provisional diagnosis of AUB were studied. Among these, 293 cases (62.34%) were D&C samples and 177cases (37.65%) were hysterectomy specimens. Bulk of the cases of about 272 (57.86%) show normal cyclical endometrium (fig 1 and fig 2)which is correlating with previous studies like Zeeba S et al[2] and Baral R et al[3].

Age Distribution:

The present study includes patients in the range of 16-66 years with mean age of 41.2 years. The maximum incidence of AUB was in the range of 41-50 years (199 patients), followed by 31-40 years age group (167 patients). Present study have found a maximum incidence of AUB in the perimenopausal age group similar to the studies of Moghal N et al [4] and Bhatta S et al [5] As women approach menopause, cycles shorten and often become intermittently anovulatory due to a decline in the number of ovarian follicles and fluctuations in the estradiol level leading to various patterns of abnormal bleeding.

Bleeding Pattern:

In the present study the predominant bleeding pattern was menorrhagia which constitutes about 296 cases (62.97%). This is correlating well with other studies like Zeeba S [1] et al. Other patterns of bleeding in this study were 110 cases of metrorrhagia (23.40%), 53 cases of post-menopausal bleeding (11.27%) and 11 cases of polymenorrhoea (2.34%). Whereas in other studies like Ayesha et al [6] the predominant pattern of bleeding was polymenorrhoea.

Various Histopathological Patterns of Endometrium:

In the present study, a proliferative pattern of endometrium was observed in 172 (36.59%) patients and secretory pattern in 100 (21.27%) patients. Other studies like Baral R et al [3]and Zeeba S et al [2] reported similar incidences of proliferative pattern. This pattern was commonly observed in the late reproductive and perimenopausal women may be due to the hormonal imbalance in this group leading to intermittent anovulatory cycles and abnormal bleeding.

Endometrial Hyperplasia:

Among the organic lesions with AUB endometrial hyperplasia was the most common histological pattern observed in our study and was seen in 61 cases (12.97%). Other studies like Baral R3 et al, Khan S[7] et al have reported a similar incidence with 18.8%, 12.6% respectively. In contrast Farquhar CM et al, Shagufta S et al showed endometrial hyperplasia only in 4.33% and 4.9% cases respectively. The reason probably being they considered only the reproductive age group whereas present study includes adolescence, reproductive age with largely perimenopausal and menopausal age groups. Therefore the effects of estrogen excess appear to be more marked in later ages.

In the present study, the maximum incidence of hyperplasia was noted in the 41-50 year age group (perimenopausal) and was seen in 32 of 61 patients (52.45%). This was consistent with the findings in other studies like Baral R[3] et al, Khan S[7] et al . Identification of endometrial hyperplasia is important because they were the precursors of endometrial carcinoma. In the present study non atypical hyperplasia (fig 3) was seen in 59 patients(96.73%) and atypical hyperplasia in 2 cases(3.27%).

Cystoglandular hyperplasia is pattern of non-atypical hyperplasia but the glands are cystically dilated and tortuous and produce the characteristic “Swiss Cheese” appearance.

Disordered Proliferative Endometrium :

Disordered proliferative endometrium is an exaggeration of the normal proliferative phase without significant increase in the overall ratio of glands to stroma and is due to persistent oestrogen stimulation. [10,11] This pattern is particularly seen in perimenopausal women. The disordered proliferative endometrium resembles normal proliferative tissue in consisting of glands lined by cytologically bland, pseudostratified, proliferative, mitotically active epithelium and in having a normal ratio of glands to stroma. It differs from the normal proliferative endometrium in the absence of uniform glandular development. This pattern was seen in 7 (1.48%) of our cases. Another study reported a incidence of 6.56%.[12]

Irregular Ripening And Irregular Shedding:

Irregular ripening and shedding are ovulatory causes of AUB and due to inadequate production of progesterone due to defect in corpus luteum. (corpus luteal defect) Irregular ripening is because of corpus luteal deficiency causing decreased amounts of progesterone and PG F2 leading to premenstrual spotting and polymenorrhoea. The endometrium shows irregular and patchy secretory changes termed as irregular ripening. [13]

Irregular shedding is attributed to a persistent corpus luteum with prolonged progesterone production and a mixed pattern of secretory and proliferative endometrium is seen after 5 days of the onset of bleeding.[13] In the present study there were 5 cases(1.06%) of irregular shedding and 7 cases(1.48%) of irregular ripening which was

common in 31-50 years age group. Similar incidence of 3.84% was seen in other studies like Shajitha K et al. [14]

Atrophic Endometrium:

Atrophic endometrium is the most common cause of bleeding in postmenopausal stage. [15] Thin walled veins, superficial to the expanding cystic glands, make the vessels vulnerable to injury and lead to excessive uterine bleeding.[3] Atrophic endometrium was seen in 31(6.59%) patients in this study which was predominant in 51- 60 year age group (15patients) followed by 41-50 years (11 patients) and they presented as postmenopausal bleeding. A similar incidence was reported in other studies.[14,15]

Pill Endometrium - (Exogenous Harmonal Effect):

In our study, pill endometrium was seen in 12 cases (2.55%). In this pattern, the endometrium shows a combination of inactive glands, abortive secretions, decidual reaction (pseudodecidual change), and thin blood vessels. This pattern was predominantly seen in the perimenopausal age group. In studies like Bhoomika D et al [16] reported a higher incidence (10%) of pill endometrium. This was probably due to increased number of patients in this age resorting to early medical management for bleeding.

Endometrial Adenomatous Polyp:

In the present study there were 29 cases of adenomatous polyp (fig 6) (6.16%) out of which 20 cases were in the perimenopausal age group (41-50 years), 7 cases were in 31-40 year age group and 2 cases in postmenopausal age. This was correlating well with other studies like Bhoomika D et al.[16] Most commonly polyps are associated with intermenstrual bleeding or spotting, but in the present study menorrhagia was the common presentation.

Chronic Endometritis:

The histological criteria for chronic endometritis include presence of plasma cells in the endometrium. Patients with chronic endometritis can present with AUB, pelvic pain and infertility. This condition needs to be diagnosed because with specific treatment, endometrium starts functioning normally. In the present study 6 cases of chronic endometritis (1.27%) were reported similar to the study done by Mazur MT et al[11] (1.3%) All the 6 cases in the present study were in the younger age group between 21-40 years. Among these 6 cases one case was associated with abortion (post abortive endometritis) and one was tuberculous endometritis (fig 5) which showed characteristic epithelioid granulomas in the endometrium. Tuberculous endometritis causes abnormal bleeding, pelvic pain and infertility. In the present study the patient was 45 years age and presented with abnormal bleeding.

Endometrial Metaplasia:

Other benign pattern observed in this study was metaplasia. Endometrium shows metaplasia in response to oestrogen, progesterone or due to irritation, trauma, polyp or chronic endometritis. The present study show 6 cases (1.27%) of metaplasia. Out of these 2 cases each of squamous metaplasia (fig 4) mucinous and eosinophilic metaplasia. Other studies like Bhatta S et al [12] showed an incidence of 6%.

Pregnancy Related Causes:

In the present study abnormal bleeding in reproductive age group was due to pregnancy related causes. This was correlating well with previous studies lik Bhatta S et al [12] (5%).In the present study there were 15 cases (3.19%) related to pregnancy. Among these, 12 cases were retained products of conception and 3 cases were complete vesicular mole.

Malignant Causes:

The malignant conditions observed in this study included 4 cases of endometrial carcinoma (fig 7,fig 8)(0.85%) and one case of low-grade endometrial stromal sarcoma. (fig 9, 10)The predominant type of endometrial carcinoma was endometrioid type which constituted 3 cases and 1 case of papillary adenocarcinoma.

Among the 3 classical cases one showed squamous metaplasia. The most common presentation in these patients was postmenopausal bleeding and incidence of endometrial carcinoma was 21.73% in the postmenopausal group. This was similar to that reported by Baral R et al [2] with an incidence of 21%.

Unsatisfactory For Evaluation:

There was very limited literature about the criteria for considering an endometrial specimen as adequate or inadequate.

In our study we had 14 cases of unsatisfactory samples among 293 D&C samples (4.77%), Most of these showed only large areas of hemorrhage and scanty glands or stroma. These were labeled unsatisfactory to report and the clinician was advised to repeat biopsy if clinically indicated.

Conclusion

Endometrial cause of AUB is age related pathology. Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of AUB and a specific diagnosis could help the physician to plan therapy for successful management of AUB.

Endometrial curettage is relatively inexpensive and safe out-patient procedure. Hormonal assay is very expensive and ultrasonography has limited role in functional causes of AUB and the findings must be correlated with the histomorphological studies of endometrium.

The disadvantage of endometrial biopsy is that it is an invasive procedure and risk of secondary infection and rarely uterine perforation.

References

1. Munro MG. Abnormal uterine bleeding in the reproductive years: Pathogenesis and clinical investigations. J Am Assoc Gynecol laparos 1999;6:393-416
2. Zeeba S. Jairajpuri, S. Rana and S. Jetley 2013. Al Ameen J Med Sci. 2013; 6(1): 21 - 28
3. Baral R, pudasini S; Journal of pathology of Nepal. 2011;1: 13-16.
4. Moghal N. Diagnostic value of endometrial curettage in abnormal uterine bleeding- a histopathological study. J Pak Med Assoc. 1997; 47:295-299
5. Bhatta S, Sinha AK ; Histopathological study of endometrium in abnormal uterine bleeding, Journal of Pathology of Nepal Vol. 2, 297-300
6. 85. Ayesha Sarwar and Anwar ul Haque; International Journal of Pathology; 2005; 3(2): 65-70
7. 88. Khan S, Hameed S, Umber A. Histopathological pattern of endometrium on diagnostic D and C in patients with abnormal uterine bleeding. Annals. 2011; 17:166-70.
8. Farquhar CM, Lethaby A, Sowter M, Verry J, Baranyai J. An evaluation of risk factors for endometrial hyperplasia in premenopausal women with abnormal menstrual bleeding. Am J Obstet Gynecol. 1999;181(3).
9. Shagufta S, Akhter S, Utman N. Causes of meorrhagia and its pathological diagnosis by dilatation and curettage. J Postgrad Med Inst 2005; 19(1): 62-65
10. Mutter GL. Diagnosis of premalignant endometrial disease. J Clin Pathol. 2002; 55: 326-31.
11. Mazur MT, Kurman RJ. Normal endometrium and infertility evaluation. In: Mazur MT, Kurman RJ, editors. Diagnosis of endometrial biopsies and cuttings: A practical approach. 2nd ed. New York: Springer Verlag; 2005; 7-33.
12. Bhatta S, Sinha AK; Histopathological study of endometrium in abnormal uterine bleeding, Journal of Pathology of Nepal. 2012; 2:297-300
13. Mehrotra VG, Mukerjee K. Pandey M. Functional Uterine Bleeing – (A Review of 150 cases) J. Obstet & Gynecol India, 1972; 22: 684-689
14. Sajitha K, Padma SK, Shetty KJ, Krishnaprasad HL, Permi HS, Hegde P. Study of endometrium in abnormal uterine bleeding. CHRISMED J health Res 2014; 1:76-81.
15. Cornitescu FI, Tănase F, Simionescu C, Iliescu D. Clinical, histopathological and therapeutic considerations in non-neoplastic abnormal uterine bleeding in menopause transition. Rom J Morphol Embryol 2011; 52:759-65.
16. Bhoomika D, Gauravi D, Amit A, Krupal P et al : histopathological study of endometrium in dysfunctional uterine bleeding. Int J Res Med. 2013;2 (1); 20-24.