



DIAGNOSTIC UTILITY OF HISTOPATHOLOGICAL PATTERNS OF ENDOMETRIUM IN ABNORMAL UTERINE BLEEDING AND ITS CORRELATION WITH AGE -A TWO YEARS STUDY AT A RURAL TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

Abnormal uterine bleeding (AUB) is a common gynaecological disorder in women of all ages caused by a wide variety of disorders. Aim of the present study was to know the different endometrial lesions in cases of AUB reported in rural tertiary care hospital and its correlation with age of presentation. This was a descriptive study which was conducted at a rural tertiary care hospital in Pondicherry. Study included endometrial curettage / hysterectomy specimens pertaining to AUB, received for a period of two years in department of pathology. Representative sections of endometrium and myometrium were taken from hysterectomy specimens and endometrial curettage were processed as a whole and slides were stained with haematoxylin and eosin. Endometrial tissues of 600 cases were studied. Age of the patient varied from 18 to 73 years. Peak incidence was seen in perimenopausal women (36-49 years). Different histopathological patterns of endometrium were observed, Normal cyclical pattern (62.8%) were more commonly seen followed by Pregnancy related complications(10.7%), disordered proliferative phase (9.5%), Endometrial hyperplasia (5.4%), Hormonal imbalance (4.3%), Benign endometrial polyp (3.6%),Atrophic endometrium (1.5%), Endometrial adenocarcinoma of endometrioid variant (1.3%), Endometritis (0.6%), Arias stella reaction (0.2%) and Pyometra (0.2%). Endometrial biopsy/ curettage are the two most important sampling methods for definitive diagnosis of endometrial pathology which can result in tailor made management of AUB, leading to rational surgical or medical intervention. In addition , it can lead to early detection and diagnosis of preneoplastic/neoplastic conditions that can minimise patient's morbidity/mortality

Keywords: *Abnormal Uterine Bleeding, endometrium, curettage, hysterectomy, biopsy, myometrium*



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INTRODUCTION

Abnormal uterine bleeding (AUB) is a common gynaecological disorder in women of all ages caused by a wide variety of disorders.¹ Endometrial diseases rank among the most common gynaecological disorders that affect women globally.² These diseases cut across all age groups and contribute significantly to increased maternal morbidity and mortality. Most females with endometrial diseases present with abnormal uterine bleeding (AUB) affecting general health of women. Thus, AUB justify the need for urgent diagnosis. This is so because of the wide range of histopathological patterns of endometrium diseases which offer diagnostic challenges to practising pathologists and thus facilitates treating clinicians. These lesions range from simple endometrial hyperplasia to more complex disorders including endometrial carcinoma. Majority of these lesions can only be diagnosed by sampling the endometrium. Endometrial biopsy and curettage are the two most important sampling methods for definitive diagnosis of the lesions. Studies have shown that a histopathological pattern of diagnosis varies with respect to the age of patients. Most young women of reproductive age present more commonly with changes associated with hormonal imbalance. However, older women of perimenopausal and postmenopausal age group present more commonly with endometrial hyperplasia and endometrial carcinoma. Thus, histopathological findings proves to be the single most important diagnostic tool for management of AUB patients. Cancer of the endometrium is the most common gynaecological malignancy in developed countries and the second most common gynaecological malignancy in developing countries after cancer of the cervix.³ Studies in the United State confirm that endometrial cancer constituted 6% of all gynaecological cancer and the third most common cause of death resulting from gynaecological malignancy after ovarian and cervical cancers. Globally, about 10% of all perimenopausal and postmenopausal women with AUB present with endometrial cancer.⁴ This paper intends to

establish a database with respect to histopathological patterns and frequencies of endometrial diseases in women of various age groups presenting with AUB at a rural tertiary care centre in South India.

MATERIALS AND METHODS

This was a descriptive study which was conducted at the Mahatma Gandhi Medical College and Research Institute, Pondicherry, a rural tertiary care hospital after obtaining permission from Institutional Human ethical committee (IHEC No.2013/54). The present study comprised of endometrial curettage / hysterectomy specimens with clinical diagnosis pertaining to abnormal uterine bleeding which was received for a period of two years in the Department of Pathology, Mahatma Gandhi Medical College and Research Institute, Pondicherry. The biopsies were analyzed with reference to clinical features, gross and light microscopic findings with special emphasis on the histological type and grade of tumors in case of malignant tumors. 600 cases of endometrial samples pertaining to AUB were received during this period. Patients with bleeding from cervico-vaginal lesion and with known haematological cause were excluded from the study.

RESULTS

During the study period of two years in Department of Pathology, MGMCR&RI from August 2012 –July 2014, 600 endometrial tissues obtained by Dilatation & Curettage (D&C) and also from hysterectomy specimens with the clinical diagnosis of abnormal uterine bleeding were studied. The age of patients in our study ranged from 18 to 73 years. Age wise histopathological patterns of endometrium in 600 cases was illustrated in the following [Table I] Majority 390(65%) belonged to perimenopausal age group followed by 128 cases (21.3%) were in reproductive age group. [Figure 1]

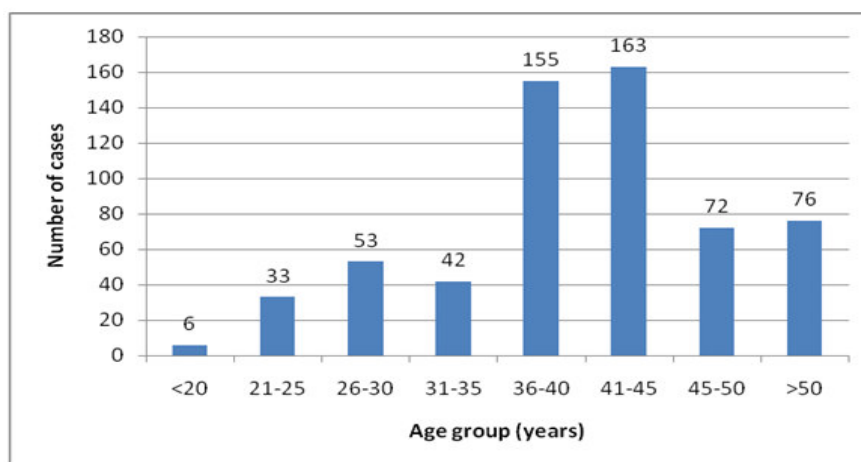


Figure 1
Age distribution pattern in 600 cases of AUB

On evaluating the causes for AUB in 600 cases based on the histomorphology of endometrium, functional cause [469/600 (78.17%)] was more common cause than the organic cause [131/600(21.83%)] In all 600 endometrial lesions [Table II], normal cyclical pattern was predominant finding observed in 377 cases (62.8%) followed by disordered proliferative phase (9.5%). Pregnancy related complications were seen in 64 cases (9.2%) which included retained decidual tissue, complete mole (1.2%) and partial mole (0.3%). Hyperplasia was observed in 32 cases(4.6%), benign endometrial polyps in 3.6% cases, endometrial adenocarcinoma in 1.3% cases, chronic endometritis in 0.4% cases, acute endometritis, aria stella reaction and pyometra in 0.2% each.

Table I
Correlation of Histopathological patterns with age distribution in women presenting with abnormal uterine bleeding

Histopathological patterns of endometrium	Adolescent (<20yrs)	Reproductive age (21-35yrs)	Perimenopausal Age (36-49yrs)	Postmenopausal Age (>50yrs)	Percentage (%)
Normal cyclical pattern	0	55(42.97%)	284(72.8%)	38(50%)	377(62.8)
Atrophic	0	0	0	9(11.8%)	57(9.5)
Disordered proliferative phase	0	9(7.03%)	42(10.77%)	6(7.89%)	9(1.5)
Hormonal imbalance	0	1(0.78%)	21(5.38%)	4(5.2%)	26(4.3)
Benign endometrial polyp	0	2 (1.56%)	13(3.3%)	7(9.2%)	22(3.6)
Simple hyperplasia without atypia	0	5 (3.9%)	20(5.12%)	3(3.95%)	28(4.7)
Simple hyperplasia with atypia	0	0	0	1(1.31%)	1(0.2)
Complex hyperplasia with atypia	0	0	1(0.3%)	2(2.63%)	3(0.5)
Retained decidual tissue	5(83.33%)	46(35.94%)	4(1.03%)	0	55(9.2)
Complete hydatidiform mole	0	6(4.69%)	1(0.3%)	0	7(1.2)
Partial hydatidiform mode	1(16.67%)	1(1%)	0	0	2(0.3)
Endometrioid adenocarcinoma	0	0	4(1.03%)	4(5.26%)	8(1.3)
Acute endometritis	0	1(1%)	0	0	1(0.2)
Chronic endometritis	0	1(1%)	0	1(1.31%)	2(0.4)
Aria stella reaction	0	1(1%)	0	0	1(0.2)
Pyometra	0	1(1%)	0	1(1.31%)	1(0.2)
Total	6	128	390	76	600

Table II
Histopathological Patterns of endometrium in 600 cases presenting with AUB

Histopathological patterns of endometrium	No of cases	Percentage (%)
Normal cyclical pattern	377	62.8
Disordered proliferative phase	57	9.5
Atrophic	9	1.5
Hormonal imbalance	26	4.3
Benign endometrial polyp	22	3.6
Simple hyperplasia without atypia	28	4.7
Simple hyperplasia with atypia	1	0.2
Complex hyperplasia with atypia	3	0.5
Retained decidual tissue	55	9.2
Complete hydatidiform mole	7	1.2
Partial hydatidiform mode	2	0.3
Endometrioid adenocarcinoma	8	1.3
Acute endometritis	1	0.2
Chronic endometritis	2	0.4
Aria stella reaction	1	0.2
Pyometra	1	0.2
Total	600	100

DISCUSSION

AUB is a commonly encountered gynaecological problem, which includes bleeding from both functional and structural cause. In most instances, functional bleeding is due to anovulatory cycle, and it is considered after the exclusion of structural, medication, psychological, iatrogenic and systemic disorders. The most common age group presenting with AUB in the present study was 4th decade of life in 65% cases. Similar observations were also made by Muzaffar, Saraswathi et al, Bhatta et al and Jairajpuri et al.^{4,5,6,7} Whereas in a study conducted by Shilpa et al showed the maximum cases were reported in 3rd decade of life.⁸ An increased number of cases in the 4th decade of life was observed due to the fact that as menopause approaches, there is decrease in ovarian follicles and their increased resistance to gonadotrophic stimulation, which decreases the oestrogen level which cannot keep the normal endometrium growing.⁹ Abnormal uterine bleeding results in well defined organic abnormality in about 25% of cases.¹⁰ In the present study, organic cause for AUB was determined in 131 (21.83%) cases. Similar findings were also observed in data published by

Vaidya S et al, Ara et al and Moghal et al.^{11,12,13} In our study, Normal cyclical pattern (68%) was the most common histopathological finding encountered, similar observations were studied by Saraswathi et al., Jairajpuri et al. Mirza T et al., and Forae et al.^{5,7,14,15} The bleeding in proliferative phase may be due to anovulatory cycles and bleeding in secretory phase is due to ovulatory dysfunctional uterine bleeding.⁵ A significant number of cases (9.5%) in our study occurred most commonly in 41-50 years of age and showed disordered proliferative phase, which was similar with the observations made by Saraswathi et al. Jairajpuri et al. and Mirza T et al.^{5,7,14} The occurrence of benign endometrial polyps in our study was seen in 3.6% cases, which was the most commonly seen organic lesion in postmenopausal age group and also in perimenopausal age group. In the younger age, the incidence of endometrial polyp is low, it may be attributed to a possibility of spontaneous regression mechanism, which is characteristic of the cyclical endometrium in reproductive age group.⁵ Non-random chromosomal aberrations and monoclonality suggests

that polyp make up a microenvironment for the development of malignancy.¹⁶In the studies that were conducted in the past, the maximum number of pregnancy related complications in AUB was reported by Forae et al (29%).and the minimum number of cases was reported by Mirza T et al (5%).^{15,14} In the present study, the incidence of pregnancy related complication was found to be 10.7% and it was predominantly seen in third decade. This can be explained by the fact that many of the women conceive at this age and the potential cause for bleeding includes spontaneous

pregnancy loss, ectopic pregnancy, placenta previa, abruptio placenta and trophoblastic disease.⁷ In the present study, seven cases had complete hydatidiform mole and two cases had partial hydatidiform mole. Various studies indicated that the occurrence of hyperplasia in AUB ranged from 5% to 18.03%.^{6,8} In the present study endometrial hyperplasia was seen in 5.4% cases which includes simple hyperplasia without atypia (in 4.7% cases)(Fig 2), simple hyperplasia with atypia (in 0.2% cases) and complex hyperplasia with atypia (in 1.2% cases) and most commonly seen in fifth decade

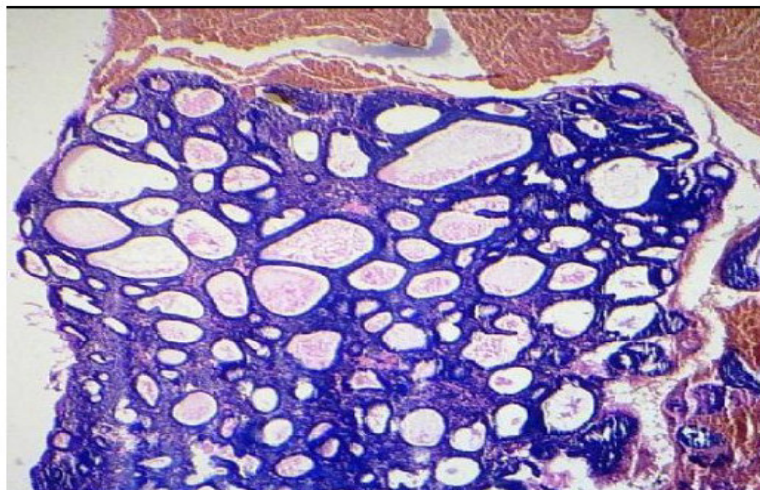


Figure 2
Simple hyperplasia without atypia with large cystically dilated glands and compact Stroma (H & E stain 4x)

The incidence of endometrial hyperplasias in this study was less as compared to other studies. The possible reason could be that most of patients here belong to lower socioeconomic status and the occurrence of risk factors like obesity, diabetes; increased intake of animal fat and sedentary life style is less. Another explanation could be that most of the patients are being diagnosed earlier stages that are in the disordered proliferative phase. Identification of endometrial hyperplasia is important because they are thought to be precursors of endometrial carcinoma.⁵In the present study, endometrial carcinoma was seen in 1.3% cases, which were seen commonly seen in ≥ 51 years of age, which

was similar to occurrence that was reported by Shilpa et al in 1% cases and Forae et al. in 1.7% cases.^{8,15} [Fig 3,4,5]. Lower incidence of 0.47% and 0.4% was reported by Jairajpuri et al. and Khan S et al. respectively.^{7,17} Likewise, higher incidence of 5.74% and 4.4 % was reported by Saraswathi et al and Bhatta et al respectively.^{5,6} A study done by Dangal et al in Nepal documented a lower incidence of endometrial cancer in Nepalese woman, reason being the practice of early childbearing and multiparity.¹⁸ Possibly, the same factors accounted for lower incidence of carcinoma in our patients.



Figure 3
Endometrial carcinoma with grey white exophytic growth occupying the endometrial cavity

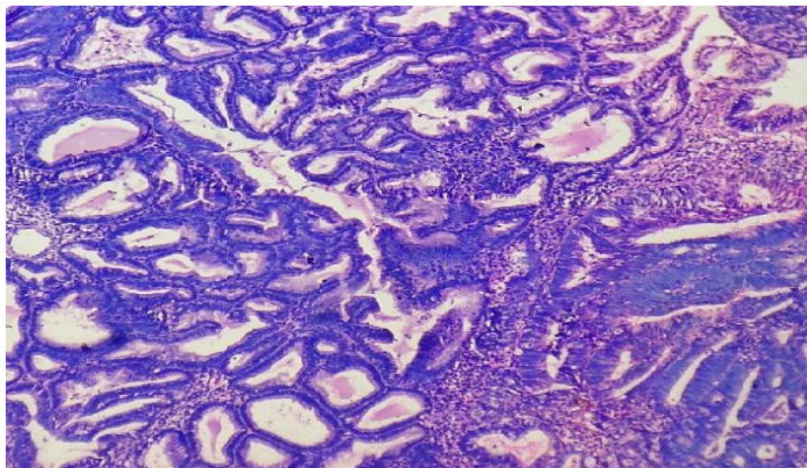


Figure 4
Endometrial adenocarcinoma (H & E stain 10x)

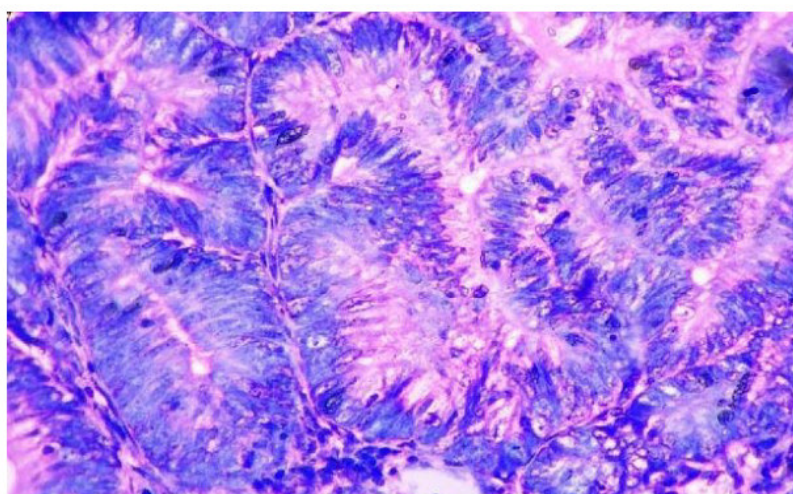


Figure 5
Endometrial adenocarcinoma- Endometrioid variant showing endometrial glands in villoglandular architecture with intraglandular bridging and scanty intervening stroma, cells are variable in size with increased stratification, loss of polarity and increased mitotic activity (H & E stain 40x)

CONCLUSION

Abnormal uterine bleeding is the commonest of all gynaecological pathology in women of all ages caused by a wide variety of disorders. Recent studies showed factors like obesity, a high-fat diet, and reproductive factors such as nulliparity, PCOS (Polycystic Ovarian Syndrome), early menarche, late menopause and HNPCC (Hereditary Non-polyposis Colorectal Cancer) syndrome is associated with a markedly increased risk of endometrial cancer compared with women in the general population. Early detection of any endometrial pathology can minimise the morbidity of

patient. Thus, endometrial biopsy/ curettage are the two most important sampling methods for definitive diagnosis of endometrial pathology which can result in tailor made management of AUB, leading to rational surgical or medical intervention. In addition, it can lead to early detection and diagnosis of preneoplastic/neoplastic conditions that can minimise patient's morbidity/mortality and also the cost incurred for the management of disease.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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