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Clinicopathological analysis of abnormal uterine bleeding in reproductive and post menopausal women in a tertiary care centre of south eastern part of India

Rupal Samal[1,*], Anandraj Vaithy[2], Shanmugasamy [2], Syed Habeebullah[1]

[1]*Dept. of Obstetrics & Gynecology, Mahatma Gandhi Medical College& Research Institute, Sri Balaji Vidyapeeth (Deemed to University), Puducherry, India*
[2]*Dept. of Pathology, Mahatma Gandhi Medical College& Research Institute, Sri BalajiVidyapeeth (Deemed to University), Puducherry, India*

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ABSTRACT

Introduction: Abnormal uterine bleeding (AUB) is a common presentation of gynecologic disorder in Tropical countries like India. Though various underlying causes exists, endometrial pathology is the major reason for AUB and histopathological evaluation of endometrial biopsy samples remains main stay for diagnosis.
Aims and Objectives: To analyse the clinico-pathological spectrum of abnormal uterine bleeding with associated endometrial lesions in patients presenting to a tertiary care hospital in south eastern part of India
Materials and Methods: Patients presenting to gynaecology OPD with AUB as presenting complaints were evaluated with Dilatation & curettage and the endometrial samples obtained were analysed for histopathological evaluation
Observations: Among 153 cases studied for a period of 2 years duration, majority of cases were non-neoplastic lesions (n=93) followed neoplastic lesions (n=60). Proliferative and secretory endometrium was the common condition among reproductive age group. Malignancy was predominantly noted among post menopausal age group and adenocarcinoma (TypeI) was the common endometrial malignancy noted
Conclusion: The incidence of Abnormal uterine bleeding was higher than assumed among the study population and histopathological evaluation of endometrial biopsy samples serves as a mainstay in diagnosis and also in categorizing the underlying etiology.

1. Introduction

The endometrium is a dynamic segment in uterine cavity of female reproductive system which reacts to various stimulus which may be physiological as well as pathological.[1] Being exposed to continuous indigenous hormonal effects, the glands and stroma undergoes many phases like proliferation, secretion, differentiation and breakdown of tissue component commonly termed as ' Menstruation'.[1,2] It starts from menarche and continues till a female attains menopause. Menstruation is the physiological cyclic process, characterized by uterine bleeding experienced by women from menarche to menopause of their reproductive age.[2,3] Normal menstruation is defined as " the bleeding under influence of progesterone from secretory endometrium which is post ovulatory characterized by stromal and glandular breakdown and shedding with a duration not exceeding five days in a regular 28 days cycle". Any bleeding per vagina not fulfilling above criteria is pathological and usually termed under the category abnormal uterine bleeding [AUB].[3,4]

Abnormal uterine bleeding is a common clinical complaints and known affect women of all age groups includingpost menopausal age.[5] The underlying etiopathogenesis of AUB is variable including non-neoplastic and neoplastic organic lesions and it varies depending on age groups as well. Many Indian studies have observed and

* *Corresponding author*.
E-mail address: rupalsamal@mgmcri.ac.in (R. Samal).

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documented that nearly two-fifth of patients presenting to Gynaecologistsin hospitals in major parts of the Tropical country present with abnormal uterine bleeding as chief clinical complaints.[5,6] Bleeding per vagina is labelled to be pathological when the pattern & flow of bleeding is constantly irregular, a ltered duration (usually >7days and irregular), or menorrhagia or increased amount of menstrual blood (>80 ml/menses).[7] As physiological age increases, the functional quality of ovarian activity declines and subsequently ovulation ceases leading to non formation of corpus luteum andthereby endometrium undergoes senile changes in form of atrophy.[8,9] As a sympathetic phenomenon, progesterone secretion is retarded due to absence of corpus luteum, leading to anovulation. i.e irregular and shortening of menstrual cycles in the climacteric phase. As as imultaneous process, there will be irregular maturation of oocytes.[10,11]

While non-neoplastic conditions including infectious lesions causes endometritis, the intensity of AUB is milder when compared with organic lesions. It had been proposed that hormonal exposure leading to mutational changes of genes (KRAS & PTEN) influences pattern of endometrial carcinomas.[11,12] Among perimenopausal age group, the etiopathogenesis of endometrial carcinomas follows a sequence of endom etrial hyperplasia with subsequent evolution of endometrial carcinoma with abnormal uterine bleeding being their mode of presentation clinically.[13]

The usual modality of approach in evaluating a case of AUB includes clinic-radio-pathological correlation.[14] However each modality has its own limitations thereby hindering on management aspects. The varied pattern of endometrial changes due to any underlying pathology could be demonstrated by novel application of analysing clinic-pathological spectrum of the conditions.[15] Dilatation & Curettage (both diagnostic and therapeutic) procedure serves as mainstay of procedural intervention in evaluation of AUB. With regard to diagnostic aspects, histopathological interpretation of endometrium by fractional curettage stays as a gold standard modality to arrive at final diagnosis to evaluate underlying etiopathogenesis aiding in further work up.[16] Hence the present study was conducted with a novel aim of analysing clinic-pathological spectrum of Endometrial curettage samples from patients presented with AUB as presenting complaints

2. Materials and Methods

The prospective study was conducted in Mahatma Gandhi Medical college & Research Institute, SBV(Deemed to be University), Puducherry for a period of 2 years duration. A Total number of 153 cases of endometrial samples obtained by Dilatation & curettage (D&C) from patients with abnormal uterine bleeding as indication were analysed for clinic –pathological spectrum.

The age, presenting complaints, relevant clinical history, detailed menstrual history, speculum examination findings, presence/absence of any polyps or lesions, etc were obtained and documented in profoma format. As a part of routine examination, D&C was done and the sample was directed to histopathology laboratory for biopsy evaluation. The biopsy samples were received fixed in 10% formalin and the gross examination was noted in terms of quantity of tissue (increased in hyperplasia and minimal in atrophic). The fixed tissue was further subjected to processing and sectioned under microtomy (4 to 5 microns thickness), stained with Hematoxylin and Eosin stain and evaluated under light microscope.

The histomorphology was divided into non neoplastic (with various sub categories) and neoplastic lesions and correlated with that of clinical parameters to categorize the endometrial patterns and changes seen in AUB.

3. Results & Observations

A total number of 153 endometrial samples obtained by Dilatation & Currettage for patients with AUB as indications were analysed for histomorphological pattern. The patients were categorized into various age groups ranging between 15 years to 75 years. Patients above 50 years were labelled as post menopausal age group and patients between 40 to 50 were categorized as perimenopausal age groups with average being 45 years.

Majority of patients fall under the reproductive age group average between 40 to 50 years of age (n=80) outnumbering Post menopausal patients (n=20). Similarly high prepond erance of perimenopausal age group in seen in non neoplastic category and hyperplasia indicating high hormonal imbalance. With regard to post menarche and early reproductive age groups, proliferative endometrium was the predominant observations followed by secretory changes. Similar observations were noted among third and fourth decade patients as well. Among perimenopausal age bleeding, proliferative endometrium topped the table and few cases of endometritis (of tuberculous origin) noted. Among post menopausal age group, most of the cases we of secretory endometrium and no proliferation noted indicating deprival of hormonal exposure. The age distribution and non neoplastic pattern was depicted in.Table 1

In respect to neoplastic category, age group above 40 dominated the table indicating underlying mutations or genetic alterations as shown in.Table 2 With regard to malignancy, predominant cases were of postmenopausal age group followed by hyperplasia (simple and complex). Varieties of pattern of malignancy was noted on macroscopic and microscopic examination with and without preceding hyperplasia as shown in.Table 3

Table 1: Agedistribution & histopathological pattern of endometrium in AUB (non neoplastic) (n=93)

Age group (in years)	PPE	Disordered PPE	SE	Irregular shedding	Endometritis Infective(TB)	Non Infectious
15-30 (n= 25)	05	01	04	-	-	–
30-40 (n= 30)	10	3	7	2	2	3
40-50 (n= 58)	25	5	11	3	1	
>50 (n=40)	–	–	3	4	–	1

*PPE- Proliferative endometrium; SE-Secretory endometrium

Table 2: Agedistribution&histopathological pattern ofendometrium in AUB (neoplastic & functional lesions)(n=60)

Age group (in years)	Hyperplasia		Polyps	Endometrial carcinoma	
	Simple	Complex		Type-I	Type -II
15-30(n=25)	3	1	2	–	–
31-40(n=30)	5	1	3	1	
41-50(n=58)	12	7	9	2	2
>50 (n=40)	1	1		5	3

Table 3: Histopathological spectrum of endometrial carcinoma (n=13)

Gross appearance	Invasion into myometrium		Preceding hyperplasia	Histomorphology
	<50%	>50%		
Ulcerative	2	4	4	Adenocarcinoma(n=4)
Polypoidal	2	3	3	Clearcell carcinoma(n= 2)
Papillarygrowth /Necrotic	1		4	Papillaryserous adenocarcinoma(n=4)
Fleshy	1		2	Carcinosarcoma (n=2)

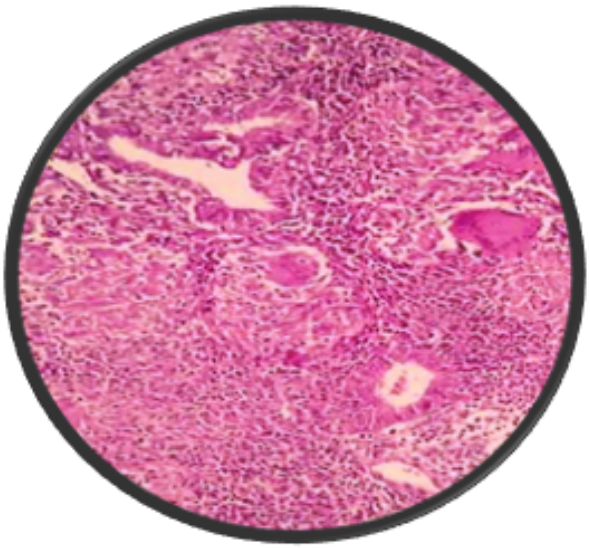

Fig. 1: Tuberculous endometritis showing granuloma with Langhans giant cell, H&E, 40X

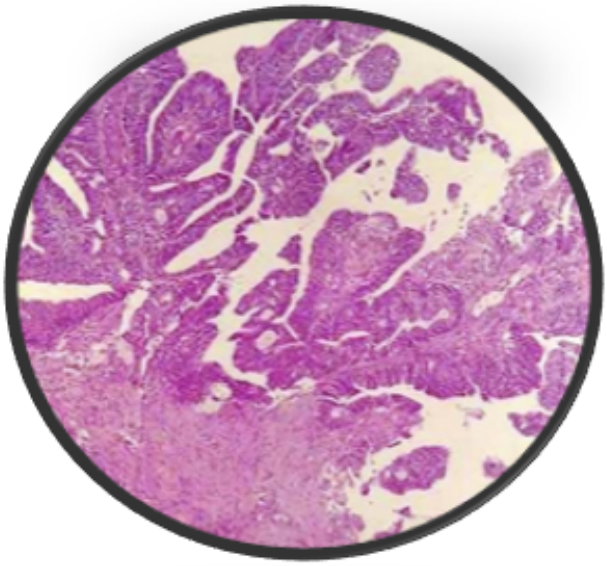

Fig. 2: Endometrial Adenocarcinoma showing glandular architecture with pleomorphism, H&E, 10X

4. Discussion

Endometrium is a dynamic portion among the female reproductive system which undergoes proliferation and shedding and regenerates as a cyclical process in response to hormonal exposure.[1,2] It changes its function as a physiological phenomenon depending on age and highly influenced by endogenous hormones. This process continues from menarche to menopause and remains as an indicator of reproductive markers for females.[3,4]

Fig. 3: Gross specimen of endometrial Adenocarcinoma showing ulceroproliferative growth with myometrial invasion

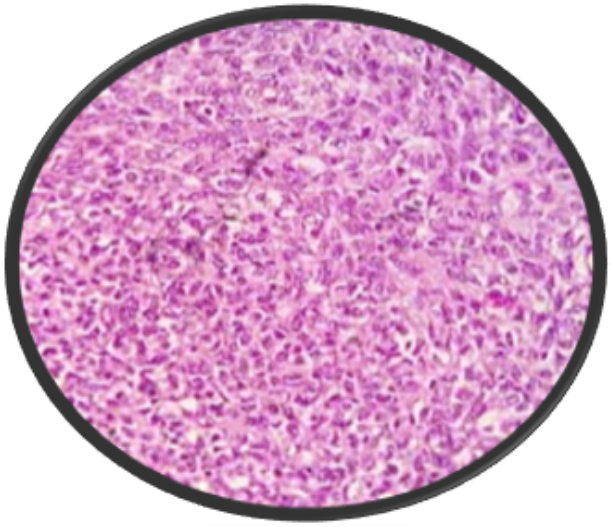

Fig. 4: Endometrial carcinosarcoma showing pleomorphic cells with mitotic activity, H&E, 40X

Any change or alterations in bleeding is termed under the broad entity 'Abnormal uterine bleeding' which is categorized depending upon duration of bleeding, amount of flow.[5,6] The amount and duration of bleeding is highly variable especially at menarche and perimenopausal as observed in this present study as well. The reason attributed is systemic in hormonal effects.[7] Bleeding occurring after menopause is termed as' post menopausal bleeding' which is usually Pathognomic and always warrants thorough evaluation both clinically and diagnostic aspects.

Evaluation of endometrial pathology is based on clinical, radiological and histopathological analysis.[8,9] Among radiological investigations, ultrasound scan is simple reliable procedure with few limitations. Hence dilatation and curettage followed by histopathological evaluation of biopsy samples is considered as a gold standard mode of evaluation for AUB.[10]

In the present study, AUB was common among reproductive age group(n= 130) especially perimenopausal age compared to post menopausal age. The observations were in concordance with study done by Muzaffaretal.[11]

The incidence of non neoplastic conditions (n=93) outnumbered neoplastic conditions. Among non neoplastic lesions, majority were of proli ferative endometrium indicating estrogen imbalance concording with observations done by Dangal, Samaletal.[12,13] Another reason proposed is anovulation in conjuction with leutal phase defect causes turbulence in feedback inhibition of pituitary secretions.

Among endometritis, the incidence was high among reproductive age group reason being usage of contraceptive device and histologically characterised by neutrophils, plasma cells and secretory stroma. Interestingly, we noted 3 cases of endometritis of tuberculous origin (Figure 1) characterized by granuloma and giant cells of langhans type with AUB associated with infertility and majority of cases fall under 3^{rd} to 4^{th} decade.

Among neoplastic and organic lesions the case incidence was 60(n=153) concording with studies done by Samal, Bhatta et al.[13,14] Based on exposure to hormones and thickness of endometrium tissue, endometriumis classified as i)hyperplasia ii) atrophy

Atrophic endometrium was noted in post menopausal age group due to deprival of estrogen stimulation concording with studies done by Samaletal.[13]

According to World Health Organisation endometrial hyperplasia are classified as simple/complex (with or without atypia) based on architectural patterns, complexity of endometrial glands and gland to stroma ratio. In the present study, majority of hyperplasia are simple and 11 cases were complex hyperplasia encountered in post menopausal age group indication mutation of genes and progression into subsequent malignancy. The observation correlated well with Kharkeetal indicating post menopausal age group as vulnerable group for malignancy[15]

Among malignancy(n=13), predominant cases were of Adenocarcinoma (Figure 2) occurring in perimenopausal and post menopausal age groups. Grossly the app earance varied from ulceroproliferative (Figure 3) to polypoidal and fleshy. Interestingly we encountered one case of carcinosarcoma in post menopausal age with fleshy gross appearance (Figure 4). The incidence and pattern of malignancy were concordant with the observations done by Dangaletal[13]

5. Conclusion

The present study enlightened on the clinicopathological spectrum of abnormal uterine bleeding in the study population. The incidence of endometrial lesions was much

higher than assumed warranting evaluation at community level. The study analysed the underlying endometrial pathology and associated lesions and emphasizes that histopathology evaluation of dilation and curettage samples plays a vital role in determining the etiopathogenesis causing abnormal uterine bleeding.

6. Source of funding

None.

7. Conflict of interest

None.

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Author biography

Rupal Samal Associate Professor

Anandraj Vaithy Associate Professor

Shanmugasamy Associate Professor

Syed Habeebullah Professor and HOD

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