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Spectrum of Histopathological Changes of Endometrium in Dysfunctional Uterine Bleeding - A Hospital Based Study

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ABSTRACT
DUB is the most common complaint in gynaecology outpatient department. Histopathological evaluation of endometrial tissue plays a significant role in the diagnosis of DUB. The study was carried out to determine the spectrum of histopathological changes of endometrial tissue in women in the age group of 20 40 years presenting with DUB. Formalin fixed specimens (endometrial curettings and hysterectomy specimens) were examined grossly, processed routinely and sections were stained with H&E stain and microscopic findings were noted. A total of 106 cases were analyzed. Normal cyclical endometrium was seen in 55(52%) cases, followed by abnormal endometrium 48(45%)cases and others(endometritis, product of conception) 3(3%) cases. Of the 55 cases of normal cyclical endometrium, proliferative endometrium was highest with 38(69%) cases, followed by secretory endometrium 13(24%) cases, anovulatory endometrium 4(7%).Out of 48 cases of abnormal endometrium,35 (73%) cases was of endometrial hyperplasia, atropic endometrium 6(13%)cases, endometrial carcinoma 4 (8%) cases and endometrial polyp 3(6%).
Histopathological evaluation of endometrial curettage and hysterectomy specimens is specially recommended in patients with dysfunctional uterine bleeding to rule out the possibility of any preneoplastic or neoplastic conditions.
Keywords: *Normal cyclical endometrium, Endometrial Hyperplasia, Endometrial Carcinoma.*

Introduction

Abnormal uterine bleeding in any period of life is considered serious and it accounts to a high percentage of outpatient department attendance. Majority of women during the reproductive age suffer from menstrual irregularities.

DUB is of considerable clinical significance because of its numerous inorganic and organic causes. Bleeding in this phase of life is of significance because of its relationship with hyperplasias and malignancies of the endometrium. To distinguish abnormal uterine bleeding from normal is at times difficult, but usually abnormal

bleeding is any deviation from the usual established cyclical menstrual pattern in an individual. The deviation may be in relation to character, amount, time and frequency. Wenz [(1)] (1988) defined abnormal uterine bleeding as any bleeding that is excessive in duration, frequency or amount for a particular patient. Cotran et al [(2)] (2010) described abnormal uterine bleeding, as excessive bleeding from the uterus during the period of menstruation or in between menstrual period. During active reproductive life, the endometrium is in a dynamic state of proliferation, differentiation and shedding, in preparation for implantation of an embryo. Menstrual cycle is exquisitely controlled by the rise and fall of the pituitary and ovarian hormones,which is executed by proper timing of hormone release in both absolute and relative amounts.Abnormalities in this system results in abnormal uterine bleeding. Although abnormal uterine bleeding can be caused by well-defined organic pathologic conditions, such as chronic endometritis, endometrial polyp, submucosal leiomyomas or endometrial neoplasms, the single group encompasses functional disturbances referred to as dysfunctional uterine bleeding. DUB is divided into two large categories: (i) Anovulatory-80% (ii) Ovulatory-20%. A hybrid group in which anovulatory and ovulatory cycles alternate is also frequently seen. History and clinical examination may not be sufficient to diagnose the cause of uterine bleeding in some cases. So histopathological examination of the endometrium is essential to formulate appropriate diagnosis for better management of patients. The objective of the present study is to interpret and compare the endometrial changes by histopathological examination of the endometrial tissue by D&C and hysterectomy specimens of patients attending the tertiary level medical facility in Guwahati

Methodology

This present study was carried out in the department of pathology, Gauhati Medical College & Hospital, Guwahati from July 2010 to June 2011, a period of one year. In this study 108 patients between 20- 40 years of age were included and all of them attended the obstetric and Gynaecology O.P.D. with the clinical diagnosis of abnormal uterine bleeding /dysfunctional uterine bleeding. The study was cleared by institutional ethical committee GMCH prior to the start of research. Written consent of the patients were taken.As usual the patients were subjected to thorough clinical examinations and routine laboratory tests and wherever required ,special investigations were also advised. In most of the cases, endometrial biopsy was performed by dilatation and curettage methods, few were of hysterectomy cases, and all possible systemic or haematological or endocrinal disorders were taken into consideration. On the basis of gross examination sections were taken from hysterectomy specimens, blood clots removed from D&C specimens and endometrial tissues processed routinely and stained with Haematoxylin and Eosin stain. Microscopic slides were viewed under low power and high power objective.

Result and Observation:

Of the 102 cases, normal cyclical endometrium was 55(52%), abnormal endometrium 48(45%) cases and others 3(3%). Of the 55 cases with normal

cyclical endometrium, 38(69%) cases showed proliferative endometrium,13(24%) cases secretory endometrium and 4(7%) cases anovulatory endometrium (cite table 1). Of the 48 abnormal cases, 35 (73%) cases were found to be endometrial hyperplasias, 6(13%) cases were atrophic endometrium, 4(8%) cases were endometrial carcinomas and 3(6%) cases were endometrial polyp(cite table2).Endometrial hyperplasias consists of simple (cystic) hyperplasia 26 (74%) cases, complex hyperplasia without atypia 7(20%) cases, complex hyperplasia with atypia 2(6%) cases (cite figure 1). The other causes of abnormal uterine bleeding in this series were endometrial carcinoma 4(4%), atrophic endometrium 6(5%) , endometrial polyp 3(3%),endometritis 2(2%) and product of conception 1(1%) (cite table 3). The cases were divided in four(4) age groups.The patients belonging to the age group of 36-40 years constituted the largest group accounting for 50% cases.The other age groups of 20-25 , 26-30 and 335 constituted 6%,16% and 28% respectively (cite figure 2). Abnormal bleeding was most common symptom which presented as menorrhagia, metrorrhagia and polymenorrhagia 1-35 constituted 6%,16% and 28% respectively (cite figure 2). Abnormal bleeding was most common symptom which presented as menorrhagia, metrorrhagia and polymenorrhagia

Table:1 Showing endometrium with normal activity

Endometrial Activity	Number of Cases	Percentage
Proliferative Endometrium	38	69.%
Secretory Endometrium	13	24%
Anovulatory Endometrium	4	7.%
Total	55	100

Table: 2 Showing Endometrial Abnormalities

Endometrial Abnormalities	Number of Cases	Percentage
Endometrial Hyperplasia	35	73%
Endometrial Carcinoma	4	8%
Atrophic Endometrium	6	13%
Endometrial Polyp	3	6%
Total	48	100%

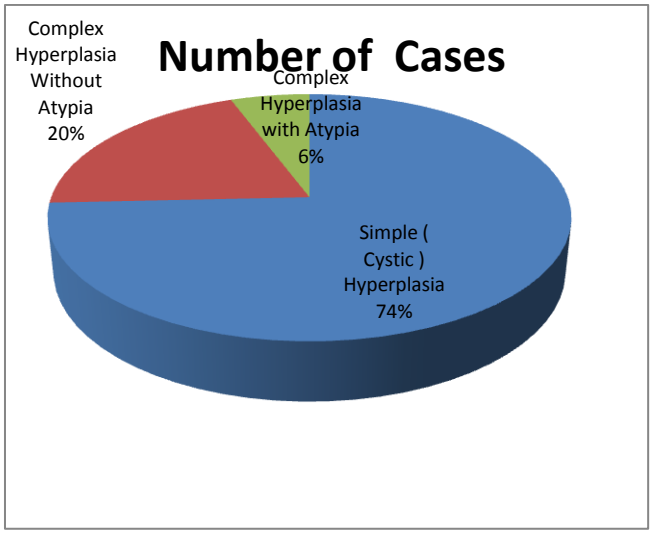


Figure :1 Showing types of endometrial hyperplasia.

Table:3 Showing different histological diagnosis

Histological Diagnosis	Number of Cases	Percentage
Normal Endometrium	55	52%
Endometrial Hyperplasia	35	33%
Atrophic Endometrium	6	5%
Endometrial carcinoma	4	4%
Endometrial Polyp	3	3%
Endometritis	2	2%
Product of conception	1	1%
Total	106	100 %

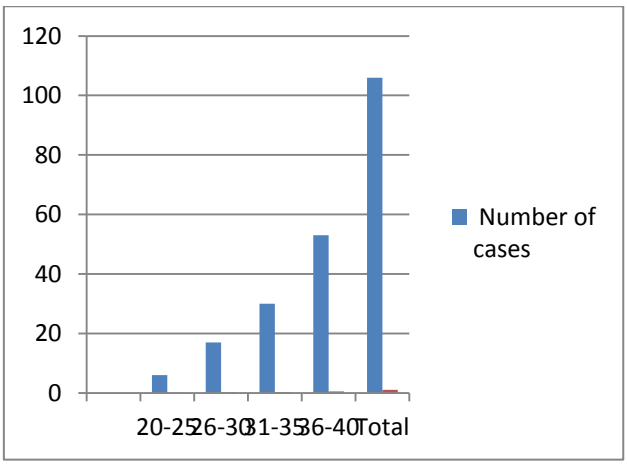
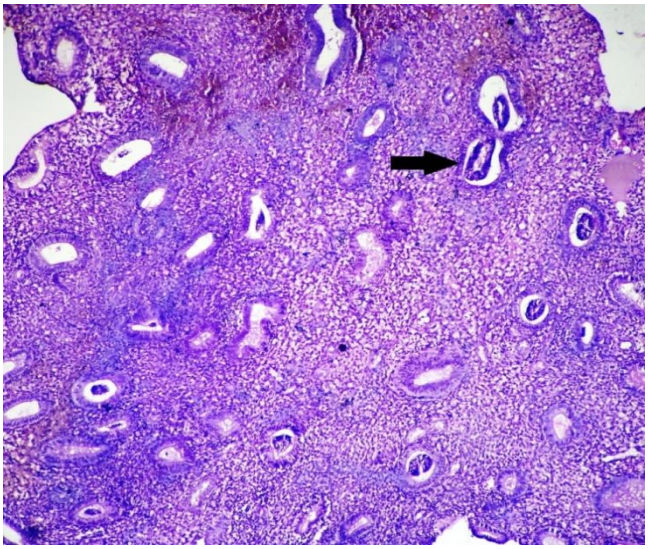
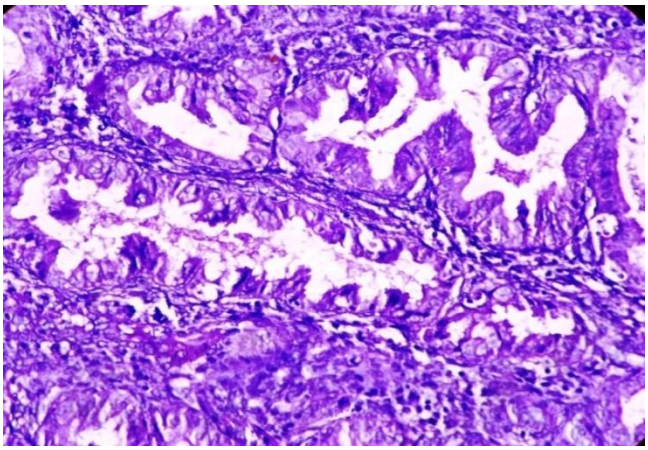


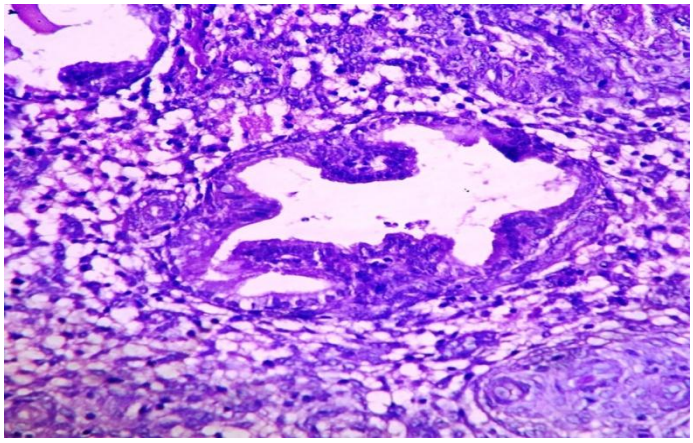
Figure: 2 Showing age group distribution.



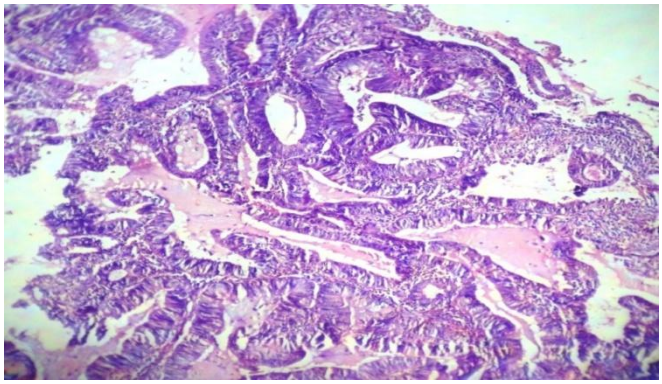
Photomicrograph Showing Histological Features Of Proliferative Endometrium.(H&E Stain, Low Power)



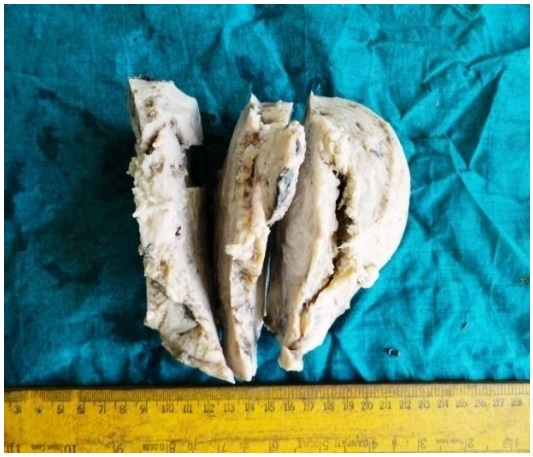
Photomicrograph Showing Histological Features Of Secretory Endometrium .(H&E Stain, High Power)



Photomicrograph Showing Histological Features Of Complexhyperplasia Without Atypia (H&E Stain, High Power)



Photomicrograph Showing Histological Features Of Endometrial Adenocarcinoma. (H&E,Low Power)



Gross Hysterectomy Specimen With Papillary Growth In The Endometrium

Discussion

In this study, the provisional diagnosis was made in 94.4% of cases following D&C and 5.6% cases following hysterectomy. Majority of women with uterine fibroid associated with menorrhagia were treated by hysterectomy. There is a wide spectrum of diseases of the reproductive system and also of the other systems that can cause abnormal uterine bleeding. It may be recalled, that in majority of the cases,no organic lesions can be identified and the diagnosis of dysfunctional uterine bleeding is made in these cases. What causes DUB, particularly in those cases where the endometrium is histologically normal remains unclear Hawkins et al [(3)]. Dilatation and curettage is fallible, but there are no adequate

data to precisely document its accuracy,not cent percent accurate Kaplan E [4]. Dilatation and curettage has a diagnostic accuracy of 80-90%. D&C is an inadequate diagnostic tool for uterine focal lesions,but the accuracy of D&C in the detection of endometrial hyperplasia and carcinoma is relatively high 92.1%. Fariba Yarandi et al [5] histologically diagnosed as normal endometrium is 52%. Other authors like Upadhya et al [6] and Baral R et al [7] histologically diagnosed as normal endometrium ;

In other studies by Samant (1969), Bhosle and Fonsena[8] (2010). However Novak[9] (1965), Michail et al (2007) found as proliferative pattern of the endometrium. In their study Khan S , Hameed S and Aneela U [10] (2011) proliferative phase of endometrium was found in 46.6% of cases. Sheetal et al 42% [11] (2009). However 54% was reported by Fakhar S et al [12] (2008). In the present study proliferative endometrium showed 69%,which is slightly higher than compared to studies by various authors.

The secretory pattern of the endometrium in this series is detected in 24% cases.This type of endometrium is called in strict terms as normal endometrium by some workers, as it is consistent with the date of the menstrual cycle, when curettage is done. Other authors like Samanth (1969) and Sheetal et al (2009) showed similar incidence, while some authors like Khan S, Hameed S and Aneela U (2011) found higher incidence 38.4%. Endometrial hyperplasia was seen in 73%, which is high compared to findings of Upadhya and Mishra [13] (1963), Carr (1969),Narula [14] (1967), Bedi [15] (1987), Baral R (2011) and Jevi Cevi [16] (1989).

The incidence of adenocarcinoma in this study was found to be 8% which is high compared with the findings of Jevi Cevi (1989) and Bedi (1987). Altthough others reported somewhat as 1.3% Sheth et al [17] (1987), 2% Shaziz F.et al (2008) and 3.3% Mencalgia [18] (1995),but it does not seem to be substancially higher. Wenz (1974) and Sherman [19] (1978) observed the incidence of endometrial carcinoma at 2.2-2.9 The risk of developing adenocarcinoma increases with age. Bride (1959) found 0.4% of cases cystic hyperplasia developed adenocarcinoma.Kelly A.Best [20] (2006) found 2.8 cases per 100,000 in the 30-34 year age group increased to 6.1 cases per 100.000 in the same age group.

In this present study incidence of endometrial polyp was found to be at 6%,which is similar to studies of various authors like Sheetal et al 5% (2009), Silander at 6.66% [21] (1962) and 7.8% by de Jong [22] (1990). An incidence of 9.8%, 10% ,12%, 20% was reported by Mencalgia (1995), Anuradha Panda (1999), Acharya Veena [23] (2003) and Jyotsana (2004). Von Theobald P, Aveline D, Levy G [24] (1991) found 17 cases of endometrial polyp. Atrophic endometrium in this series was found to be at 13%. Literature reports show quite a variable incidence observed by Nirula (1967), Jong PD et al 5% (1990), Shazia Fakher et al 8% (2008), Valle [25] 9.67% (1981) and studies of Acharya V, Mehta S.,Render A (2003) showed similar incidence of 12% and Michail et al (2007) found higher incidence of atrophic endometrium at 21.9%. von Theobald P,Aveline D,Levy G (1991) found 19 cases of atrophic endometrium. Endometritis was found in 2% cases which is quite less compared from that

reported by Shazia F et al (2008) as 3%, Silander T (1962) as 3.28% and Valle RF (1981) as 7%. Von Theobald P et al (1991) found 6 cases of endometritis.

In the present study of endometrial hyperplasia, 74% of cases was of simple hyperplasia, 20% complex hyperplasia without atypia and 6% complex hyperplasia with atypia. Wentz (1974), Sherman (1978) found in their studies the relative frequency of different types of hyperplasia as simple hyperplasia 4.8- 5.6 %, complex hyperplasia as 2.4-2.9%. Literature reports show variable incidence of endometrial hyperplasia, barel R et al (2011) found simple hyperplasia without atypia 8%, simple hyperplasia with atypia 3%, complex hyperplasia without atypia 3% and complex hyperplasia with atypia 1%. Silander found it to be 6.66%. Wentz and Behnamfar et al report it as 9% and 10.9% in their studies (2004). However Amera et al report it 15% (2009), and Dexus (1984) and Jyotsana (2004) report an incidence of 21% and 22.66%. A rather high incidence of 26% and 28.3% was reported by Sheth (1989) and Anuradha Panda (1999). Khan S. Hameed S and Aneela U.(2011) observed Cystic hyperplasia without atypia in 6.4% and with atypia in 2.4% of cases, and adenomatous hyperplasia without atypia was observed in 2.8% and with atypia in 1.0% of cases.

The highest incidence of abnormal uterine bleeding in this series is in the age group of 36-40 years with a percentage of 50%. Devi and Sutaria (1964) observed the highest incidence in the age group of 21-39 years at 43.4%. Baral et al (2011) observed in the age group of < 40 years at 23%. In this study, menorrhagia is the commonest type of presentation having the percentage of 86%. 9% of patients presented with Polymenorrhagia and 5% with Metrorrhagia. The main presenting complaint was menorrhagia (57.8%), followed by irregular P/V bleeding (32.8%) Khan S,Hameed S, Aleena U,(2011).

Conclusion

Dysfunctional uterine bleeding is usually due to endometrial cause and is mostly age related. Histopathological examination by dilatation and curettage is a major diagnostic tool in evaluation of dysfunctional uterine bleeding to rule out the possibility of any premalignant or neoplastic conditions and specific diagnosis could help the clinician to plan the mode of treatment and successful management of abnormal bleeding.

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