

## Study of endometrial tissue in dysfunctional uterine bleeding

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### ABSTRACT

Dysfunctional uterine bleeding (DUB) is defined as heavy and or irregular menstruation in the absence of recognizable pelvic pathology, pregnancy or general bleeding disorder. Hyperplastic endometrium is abnormal histology finding found in DUB. Out of three type of hyperplasia, atypical type is associated with co-existent ca endometrium and the chance of progression to ca endometrium is very high. Thus this study was conducted to see the incidence of hyperplasia of endometrium in cases of DUB and to see the risk factors for endometrial hyperplasia. It was a prospective study carried out in span of two years (2010 JULY- 2013 Jan) in Nepal Medical College and Teaching Hospital. Hundred cases DUB who under went D&C or hysterectomy were included to study the age range, the relation of parity, patient symptom, contraceptive method and medical disease with the type of endometrial histology. It was found that DUB was common in perimenopausal age (49%) and the incidence increase with the increase of parity. Abnormal endometrial finding (hyperplasia) was found in 31% of the cases. Atypical and complex hyperplasia were associated with irregular menstruation and one third of the hyperplastic patient had hypertension (32.26 %). Thus perimenopausal age, irregular menstruation and hypertension are risk factors for hyperplasia. So it is mandatory to do endometrial sampling in cases of perimenopausal age with irregular menstruation with or without hypertension.

**Keywords:** Endometrial tissue, DUB, Hyperplasia.

### INTRODUCTION

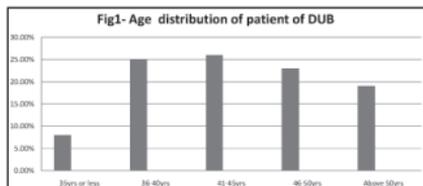
The normal menstrual cycle is defined as having a mean interval of 28 +/- 7 days with a mean interval of 4 +/- 3 days.<sup>1</sup> The upper limit of normal menstruation is 80ml per menstruation.<sup>2</sup> Any variation from the normal cycle and the amount of loss is considered abnormal uterine bleeding. Dysfunctional uterine bleeding (DUB) is one of the commonest cause of abnormal uterine bleeding. It is defined as heavy and/ or irregular menstruation in the absence of recognizable pelvic pathology, pregnancy or general bleeding disorder. It affects 20 to 30% of women<sup>3</sup> and accounts for 12% of gynaecological referrals.<sup>4</sup> DUB can be ovulatory or anovulatory. Anovulatory DUB occurs at extreme reproductive age (adolecence and perimenopausal age). The exposure of endometrium to continuous oestrogen unopposed by progesterone can lead to endometrial hyperplasia which is premalignant condition of uterus. There are three types of endometrial hyperplasia. The simple hyperplasia is the most common type which isn't associated with endometrial carcinoma and progression to endometrial cancer is only 0.4%.<sup>5</sup> The Adenomatous type is second commonest type which isn't also associated with co-existent endometrial cancer but the chance of progression to endometrial cancer is 0 to 26.7%.<sup>5,6</sup> Where as Atypical endometrial hyperplasia is associated with co-existent carcinoma rate range from 25 to 50%<sup>7</sup> and the rate of progression to cancer is 22.6% to 88.9%.<sup>8</sup> The diagnosis

of endometrial hyperplasia should be suspected in with heavy, prolong, frequent and irregular uterine bleeding in perimenopausal age. Diagnostic dilatation curettage is the gold standard method for detecting endometrial abnormality in DUB and should be done to exclude hyperplasia and malignancy in all cases of DUB in perimenopausal age. Endometrial cancer is the third most common malignancy of the female genital tract with age standardized incidence of rate of 2.9 per 100,000 women.<sup>9</sup> Abnormal uterine bleeding in perimenopausal age is the commonest symptoms of endometrial neoplasia, although such bleeding is usually 80% due to benign condition.<sup>10</sup>

This study was carried out to find out different histopathological pattern of endometrium in DUB, the prevalence of each type of endometrial hyperplasia and associated risk factors which will help us to know magnitude of the problem in our country so that strategies could be made for early prevention and intervention to prevent morbidity and mortality due to DUB.

### MATERIALS AND METHODS

This was a prospective study carried out between 2010 July till 2013 January in Nepal Medical College Teaching Hospital. One hundred patient who underwent diagnostic dilatation and curettage or hysterectomy with diagnosis of DUB were included. Detail history of the patient,



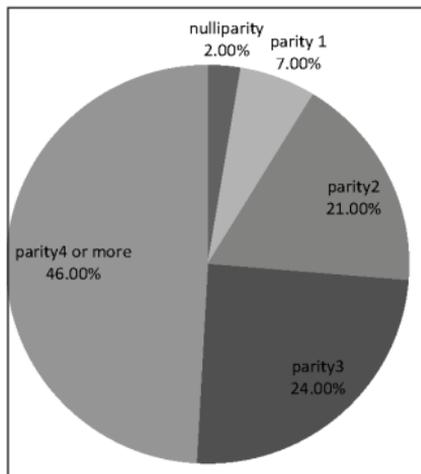
examination, ultrasound and other required investigations was carried to exclude the organic pathology, pregnancy, bleeding disorder and thyroid dysfunction. The age, parity pattern of bleeding, associating symptoms, contraceptive method, any medical history such as diabetes or hypertension was recorded. The histopathological report was obtained from pathological department. After histology report, if there was any organic pathology found such as fibroid, adenomyosis, they were excluded. Then statistical analysis was done with data obtained correlating with age, parity, pattern of bleeding and histology report.

## RESULTS

Total 100 patient with DUB who under went either D & C or hysterectomy were included in the study. Among them 45 under went D&C and 53 under went hysterectomy. The age range was 32 to 55 years (Fig. 1). We can see that DUB is maximum in age group 41-45 years 26% and minimum in the age group 35 or less than 35years 8% showing that DUB is more common in perimenopausal age than in reproductive age (49% vs33%). Table-1 gives the parity distribution. Again the incidence of DUB increase with increase of parity. Parity 4 or more were associated with DUB in 45% patient where as parity 1 were only 7%. Only 2% patient were nulliparous. The pattern of bleeding and associated symptoms were depicted in Table-1. 46% patient had irregular bleeding, 28% patient had heavy bleeding, 20% had prolong bleeding and 6% had intermenstrual bleeding. Along with DUB 60% had dysmenorrhea and 4% had significant per vaginal discharge. As regard to medical disease 15% had hypertension and 7% patient had diabetes. 4% patient had both diabetes and hypertension. Bilateral tubal ligation was done in 22%.

**Table-1:** Pattern of bleeding and associated symptoms in cases of DUB

Patient symptoms	n. (%)
Irregular bleeding	46 (46.0%)
Heavy bleeding	28 (28.0%)
Intermenstrual bleeding	6 (6.0%)
Prolong bleeding	20 (20.0%)
Dysmenorrhea	60 (60.0%)
Per vaginal discharge	4 (4.0%)



There were 17% patient with hypertension, 7% patient with Diabetes and 3% patient with both hypertension and Diabetes. When histological finding of the patient was analysed it was found that 31% patient had hyperplasia, 37% patient had proliferative endometrium, 16% patient had secretory endometrium and 10% patient had inactive endometrium. Among the hyperplasia 23% had simple hyperplasia, 5% had complex hyperplasia and 3% had atypical hyperplasia. When histopathological finding was analysed with the age of patient it was found that normal finding was found in younger age group and as the age of patient increase more pathological histological report was found (Table-2). Among the hyperplasia 21% patient were 46years or more. Among the atypical hyperplasia all 3% were in age group 46 or more than 46 years. As for the relationship of medical disease with hyperplasia, it was found that 10 (32.26%) of patient with hyperplasia, had hypertension and only 1(3.23%) had diabetes (Table-5).

## DISCUSSION

DUB is one of the commonest condition for which patient seek medical consultation. The prevalence increase with the increase age peaking prior to menopause. The perimenopausal women have anovulatory cycle leading to DUB.

**Table-3:** Types of Hyperplasia

Types of hyperplasia	
Simple Hyperplasia	23.00%
Complex Hyperplasia	5.00%
Atypical Hyperplasia	3.00%

**Table-4:** Relationship of pattern of bleeding with types of hyperplasia

Type of Hyperplasia	Irregular Bleeding	Heavy Bleeding	Prolong Bleeding	Intermenstrual Bleeding
Simple Hyperplasia	2(6.46%)	17(53.13%)	2(6.46%)	2(6.46%)
Complex Hyperplasia	4(12.90%)	1(3.23%)	0(0.00%)	0(0.00%)
Atypical Hyperplasia	3(9.68%)	0(0.00%)	0(0.00%)	0(0.00%)

In our study maximum of the patient were in perimenopausal group (49%) showing that DUB is common in perimenopausal group than in reproductive age (33%). In the study done by Sutherland (1950)<sup>11</sup> 36.21% of the patient with DUB were in perimenopausal age and 34.3% in reproductive age. Maximum of our cases were Parity 4 or more (45%) showing that higher the parity higher the incidence of DUB. In the study done by Mehrotra et al<sup>12</sup> they found that 46% were multiparous and 34% were grand multipara. The higher parity with DUB may be because of general population shows higher incidence of multiparity.

In our study 46% had irregular bleeding, 28% had heavy bleeding. Similar finding was found in Mehrotra 52% vs 29%.<sup>12</sup> Almost one third of our patient (22%) had under gone bilateral tubal ligation. Many authors have investigated the sequelae of developing menstrual abnormalities following tubal ligation. Heavy bleeding and increase dysmenorrhoea has been reported by many studies.<sup>13</sup> Peterson et al also found that after bilateral tubal ligation there is increase incidence of menstrual abnormalities.<sup>14</sup> It may be due to extensive destruction of oviduct carried by unipolar cauterisation leading to interference of blood flow in ovaries leading to

**Table-5:** Relationship of type hyperplasia with medical disease

Type of Hyperplasia	Hypertension	Diabetes	Both
Simple Hyperplasia	4(12.90%)	1(3.23%)	0(0.00%)
Complex Hyperplasia	3(9.68%)	0(0.00%)	0(0.00%)
Atypical Hyperplasia	3(9.68%)	0(0.00%)	0(0.00%)

**Table-6:** Relation of histopathological findings with the age of the patient

Age group	Simple hyperplasia	Complex hyperplasia	Atypical hyperplasia	Proliferative	Secretory	Atrophic	Irregular shedding	Pill induce
35 or less				6.00%	2.00%			
36-40yrs	5.00%			13.00%	4.00%	1.00%	1.00%	1.00%
41-45yrs	5.00%	2.00%		11.00%	6.00%		2.00%	
46-50yrs	10.00%	2.00%	2.00%	3.00%	2.00%	2.00%	2.00%	
Above 50yrs	3.00%	1.00%	1.00%	4.00%	1.00%	7.00%	1.00%	

leuteal phase defect followed by anovulation. As regard to histopathology report, 31% were hyperplasia and 50% were normal. Atrophic endometrium was 10%. The incidence of atrophic endometrium in associated with DUB in study done by

Davey (1995) was 1.9-21.9%. Atrophic endometrium is associated with large dilated venules situated superficially under thin endometrium. These venules may rupture causing abnormal uterine bleeding.<sup>15</sup> Out of hyperplasia, 74.19% was simple hyperplasia. This finding was comparable with the study done by Punitpong (2002). In his study, 34.19% was normal endometrium, 28.07% was hyperplasia, 12.90% was atrophic, and 0.97% was endometrial cancer.<sup>16</sup> There was no endometrial carcinoma in our study. Danggal reported the incidence of carcinoma 7.1%.<sup>17</sup> In the study of endometrial tissue of abnormal uterine bleeding. There was't any case of cancer endometrium probably because we have excluded the postmenopausal and probably large sample size of the patient is required to detect the cases of cancer. When analysis of patient with hyperplasia with pattern of bleeding was done, it was found that complex and atypical hyperplasia are associated with irregular bleeding 4 (12.90%) and 3(9.8%) where as in simple hyperplasia only 2 (6.45%) had irregular bleeding. Maximum of the patient with simple hyperplasia had heavy bleeding (53.13%). Again when analysis of medical disease was done with cases of DUB, We can see that 32.26% of the patient with hyperplasia were hypertensive. Takrim et al (2009) also found that hypertension was common (20%) in cases of hyperplasia.<sup>18</sup> Ash et al evaluated the the predictive value of risk factor for abnormal endometrial found that age above 40 years, irregular menstruation and hypertension are independent risk factor for abnormal endometrial histology report.<sup>19</sup>

From the above study we can see that the risk to abnormal endometrial report are mainly 40 years or above 40 yrs, irregular menstruation and hypertension. Presence of irregular menstruation after 40 yrs will

warranty evaluation of endometrial tissue. But larger sample size should be included to know the prevalence of malignancy. Diagnostic dilation and curettage (D&C) is the gold standard method of sampling of endometrial tissue. In substitute to this method, pipelle and Vibra aspiration are few methods which are simpler, cost effective outdoor procedure. Hysteroscope guided endometrial biopsy is also another alternative procedure. In addition to inspection to endometrial cavity biopsy of abnormal looking endometrium can be taken safely and accurately.<sup>20</sup> Furthermore, colour Doppler USG is an efficient axillary examine method in diagnosing endometrial hyperplasia and useful in patient follow up as each type of endometrial hyperplasia has its own characteristics in colour Doppler USG and very good tool.<sup>21</sup> Bakos in his study found that Doppler transvaginal USG could detect 76% of endometrial abnormalities.<sup>22</sup>

When endometrial hyperplasia detected then, exogenous oestrogen should be stopped and oestrogen producing ovarian tumour if present should be removed. Medical and surgical treatment should be carried out depending upon the severity of the disease, age of the patient and patients desire for children.

DUB is more common in perimenopausal age, multiparity and those patient who had under gone tubal ligation. Commonest normal histology of DUB is proliferative endometrium. One third of the patient had abnormal histology report which is found more in perimenopausal age. Irregular bleeding and hypertension is associated with hyperplasia. So perimenopausal age, irregular bleeding and hypertension are risk factor for hyperplasia. Endometrial study is mandatory to exclude premalignant and malignant condition of endometrium if one or more risk factor are present in cases of DUB.

#### REFERENCES

- Mary E, Kimza MD. Dysfunctional uterine bleeding. *Pediatr Review* 2002; 23: 227-33
- Rybo G. Clinical and experimental studies on menstrual on menstrual blood loss. *Acta obstetrica et Gynaecologica Scandinavica* 1966; 45(supply):1-23
- Cooper KG, Parkin DF, Garratt AM *et al*. A randomised comparison of medical and hysteroscopic management in women consulting a gynaecologist for treatment of heavy menstrual loss. *Brit J Obstet Gynaecol* 1997; 104: 1360-6.
- Cooke I, Lethaby A, Farquhar C. Antifibrinolytics for heavy menstrual bleeding (Cochrane Review). In Cochrane Library. Issue 3 Oxford: Update Software 1999.
- Lindahl B, Wilen R. Spontaneous endometrial hyperplasia. A prospective, 5 years follow up of 246 patients after ablation only, including 380 patients followed up for 2 years.
- Anticancer Res* 1994; 14: 2141-6. Wentz W B. Progesterin therapy in endometrial hyperplasia. *Gynaecol Oncol* 1974; 2: 362-7.
- Widra EA, Dunton CJ, McHugh M *et al*. Endometrial hyperplasia and the risk of carcinoma. *Int'l J Gynaecol Cancer* 1995; 5: 233-5.
- Kurman R, Kaminski PF, Norris HJ. The behavior of endometrial hyperplasia: a long term study of untreated hyperplasia in 170 patient. *Cancer* 1985; 56: 403-12.
- Benjachai W. Corpus uteri. In: Deerasamee S, Martin N, Sontipong *et al* editors. *Cancer in Thailand* vol.11. 1992-1994. LYON : IARC. 1999; 60-1
- Goldstein SR. Mennorrhagia and abnormal uterine bleeding before the menopause. *Best Pract Res Clin Obstet Gynaecol* 2004; 18: 59-69.
- Sutherland AM. Recent Advances in Obstetrics and Gynaecology. 1962; 365-81.
- Mehrotra VG, Mukerjee K, Pandey M. Functional Uterine Bleeding-(A Review of 150 cases). *J Obstet Gynecol* 1972; 684-9.
- Gentile GP, Kaufman SC, Helbig DW. Is there any evidence of post-tubal sterilization syndrome? *Fertil Steril* 1998; 69: 179-86.
- Peterson HB, Jeng G, Folger SG *et al*. US collaborative Review Sterilization Working Group. The risk of menstrual abnormalities after tubal sterilization. *New Engl J Med* 2000; 1681-7.
- Davey DA. Dysfunctional uterine bleeding. Chapter40 in Deherst 's test book of Obstetrics and Gynaecology for post graduates. 5<sup>th</sup> edition, 1995: 590-608.
- Puntipong B. Histology of endometrial curettings from women with abnormal uterine bleeding: 5 years retrospective study in prapokkiao Hospital. *J Prapokkiao Hospital Clin Med Edu Center* 2002; 19: 2.
- Dangal G. A study of endometrium of patient with abnormal uterine bleeding at Chitwan valley. *Kathmandu Univ Med J* 2003; 1: 110-2.
- Takreem A, Danish N, Razak S. incidence of endometrial hyperplasia in 100 cases presenting with polmenorrhagia\menorrhagia in perinopausal women. *J Ayub Med Coll Abbottabad* 2009; 21: 60-3.
- Ash SJ, Farrell SA, Flower Dew G. Endometrial biopsy in DUB. *J Reprod Med* 1996; 41: 892-6.
- Van Dongen H, de Kroon CD, Jacobi CE *et al*. Diagnostic hysteroscopy in abnormal uterine bleeding: a systematic review and meta-analysis *Brit J Obstet Gynaecol* 2004; 114: 664.
- Wang D, Wang F, Long X *et al*. Corellation analysis of endometrium ultrasound image and pathologic diagnosis in peri-menopausal patient with functional uterine bleeding. *Chinese J Obstet Gynaecol* 2010; 2: 11.
- el-Ahmadly O, Gad M, el-Sheimy R *et al*. Comparative study between sonography pathology and UGP in women with perimenopausal bleeding. *Anticancer Res* 1996; 16: 2309-13.