

## Clinicopathological Evaluation of Thyroid Dysfunction in Women with Abnormal Uterine Bleeding

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### Abstract

**Introduction:** Abnormal uterine bleeding describes any variation from normal bleeding patterns in nonpregnant, reproductive-aged women beyond menarche lasting for at least 6 months. Regular cyclic menstruation results the choreographed relationship between the endometrium and its regulating factors. Any type of disturbance between the regulatory mechanism of pituitary ovarian axis or pelvic diseases results in abnormal uterine bleeding. Thyroid hormones play a key role in the menstrual and reproductive function of women. It is recognized universally that menstrual disturbances may accompany clinical alterations in thyroid function. **Objectives:** To evaluate the thyroid dysfunction in patients with abnormal uterine bleeding. **Materials and Methods:** This cross sectional study was conducted in Department of obstetrics & gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from April 2023 to December 2023. Women with abnormal uterine bleeding were included in the study. Sample was selected by purposive sampling. Sample size was 100. Detail demographic data were collected from the informant and recorded in structured case report form. Clinical examination and relevant investigation were done meticulously. Data was collected by using a semi-structured questionnaire. Data was processed and analysed with the help of computer program SPSS and Microsoft excel. Quantitative data expressed as mean and standard deviation and qualitative data as frequency and percentage. Result was presented in the form of tables, pie chart, graphs, bar diagrams, histogram & charts etc. **Results:** In this study, the maximum numbers of cases (43.0%) were between 26-35 years age group. Mean age was  $29.57 \pm 8.27$  years. Large numbers of respondents came from urban area (58%). On evaluation of types & causes of AUB, maximum patient belongs to AUB-L (leiomyoma) group (53%) followed by AUB-A (adenomyosis) (28%); AUB-P (polyp) (8%); AUB-O (ovulatory) (9%) and AUB-M (malignancy) (2%). Present study showed that prevalence of thyroid disorders is 26% in AUB patients. The prevalence of Hypothyroidism was 18% and Hyperthyroidism was 8%. Thyroid dysfunction is associated with menstrual abnormalities in females of all age groups. **Conclusion:** Abnormal uterine bleeding has a strong association with thyroid disorders. The most common type of disorder is subclinical hypothyroidism. Thus, all patient of AUB must be evaluated for thyroid dysfunction.

**Key words:** Thyroid dysfunction, Abnormal Uterine Bleeding.

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### Introduction

Abnormal uterine bleeding (AUB) may be acute or chronic and is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency or duration and occurs in the absence of pregnancy. AUB is a common crippling gynaecological

condition with vast financial implications. A structured approach for establishing the cause using the FIGO defined PALMCOEIN (Polyp, Adenomyosis, Leiomyoma, Malignancy (and hyperplasia), Coagulopathy, Ovulatory disorders, Endometrial, Iatrogenic and Not otherwise classified) classification system will facilitate accurate diagnosis and inform treatment options<sup>1</sup>. AUB frequently co-exists with fibroids, but the relationship between the two remains incompletely understood and in many women the identification of fibroids may be incidental to a menstrual bleeding complaint<sup>2</sup>. It includes oligomenorrhoea, polymenorrhoea, hypomenorrhoea, menorrhagia, metrorrhagia and abnormal uterine bleeding. Prevalence of menorrhagia is highest between the ages of 25-34 years<sup>3</sup>.

The FIGO classification for AUB refers to reproductive-aged, nonpregnant women, so the first step is to evaluate for pregnancy and address whether a woman is premenopausal and postmenarche. Bleeding before menarche, after menopause, and during pregnancy requires different evaluations. In addition, a thorough history will help distinguish gynecologic causes of bleeding from those with urinary or gastrointestinal etiologies<sup>4</sup>. Structural causes include fibroids, polyps, endometrial carcinoma, and pregnancy complications.

FIGO System 1 describes the 4 parameters of menstrual bleeding: regularity, frequency, duration, and volume. Normal menstrual bleeding is defined as cycles that occur every 21 to 35 days. Regular menstrual bleeding should be 9 days or less in variation from the beginning of one menses to the beginning of the next one; however, this is age dependent so that women between 26 and 41 years old should have variation of 7 days or less in menstrual cycle length<sup>5</sup>. For frequency terminology, amenorrhea is when menses are absent or a woman experiences no bleeding, frequent menstrual bleeding is when menses occur less than 21 days apart, and infrequent menses is when menses occur more than 35 days apart. For duration, more than 8 days of bleeding is considered prolonged menses. Volume is harder to measure: menses are determined by women to be heavy, normal, or light. Heavy menstrual bleeding is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional quality of life<sup>6</sup>. It can occur alone or with other symptoms. Intermenstrual bleeding is bleeding between spontaneous, predictable menses and may occur randomly through the cycle or predictably and cyclically in early, mid, or late cycle. Breakthrough bleeding may occur on hormone medications such as birth control pills/patches/rings or progesterone-only contraceptives<sup>7</sup>. The PALM-COEIN classification is used herein as a systematic approach to clarifying AUB, focusing on specific evaluation and management

strategies<sup>7,8</sup>.

It has long been recognized that thyroid dysfunction may have profound effects on the female reproductive system. A relationship between the thyroid gland and the gonads is suggested by the far more frequent occurrence of thyroid disorders in women than in men and by the common appearance of goiter during puberty, pregnancy and the menopause. Thyroid disorders are more common in women with menstrual irregularities as compared to general population. The menstrual irregularities are significantly more frequent in patients with thyroid dysfunction and may precede thyroid dysfunction<sup>9</sup>.

Wiksten<sup>10</sup> established linkages between menstruation and thyroid disease. There may be various types of menstrual disorder in a case of thyroid disease. In hypothyroid patients the menstrual abnormality is much more severe and anovulatory cycles are common. Menorrhagia and metrorrhagia are most common complaints while amenorrhoea is seen rarely<sup>11</sup>. Although literature says that menorrhagia is more common in hypothyroidism and amenorrhoea or oligomenorrhoea in hyperthyroidism, but according to the study any type of menstrual irregularity can occur with either hypo or hyper function of the thyroid<sup>12</sup>.

A descriptive cross-sectional study reported that out of the total cases of AUB, 15 (15.79%) had thyroid dysfunction. Among total cases, 80 (84.21%) were euthyroid. The mean age of the patients was 33±8 years. Among thyroid dysfunction, 9 (60.0%) were hypothyroid, 4 (26.66 %) were subclinical hypothyroid, and 2 (13.33 %) were hyperthyroid<sup>13</sup>. Another study reported thyroid disorders are common in females with subclinical hypothyroidism as it's the most common type. Menstrual irregularities are seen in both hyperthyroidism as well as hypothyroidism<sup>14</sup>. The mechanism by which the hypothyroidism can affect the menstrual cycle is not fully understood. However, some authors attributed this relationship to irregular or no ovulation that decreases the luteinizing hormone and elevating the estrogen leading to menstrual bleeding.

#### Materials and Methods:

This cross sectional study was conducted in Department of obstetrics & gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from April 2023 to December 2023. Women with abnormal uterine bleeding (AUB) in reproductive age group were study subject. Women who are on drugs or hormone therapy, intra uterine device users and history of bleeding disorders were excluded. Sample was selected by purposive sampling technique. The study protocol included a thorough history taking regarding age, bleeding pattern, onset, duration, quantity of bleeding

and complaints related to thyroid dysfunction were noted in detail. A thorough clinical examination including general physical examination, neck examination, systemic and gynecologic examinations was done meticulously. All the recruited patients subjected to routine investigations like hemoglobin, ESR, LFT, Random blood sugar, complete urine examination, bleeding time, clotting time, chest x-ray, ultrasound abdomen and pelvis, pap smear, endometrial biopsy. Then all patients subjected to T<sub>3</sub>, T<sub>4</sub> and TSH. T<sub>3</sub> and T<sub>4</sub> were assayed by same laboratory by same technique in BSMMU. Patient data, clinical & laboratory findings were noted and correlated. The collected information were entered and analyzed by using SPSS v 22. Quantitative variable was presented in the form of mean and standard deviation and frequency and percentages calculated for qualitative variables. All collected questionnaire checked very carefully to identify the error in the data. Data processing work consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.

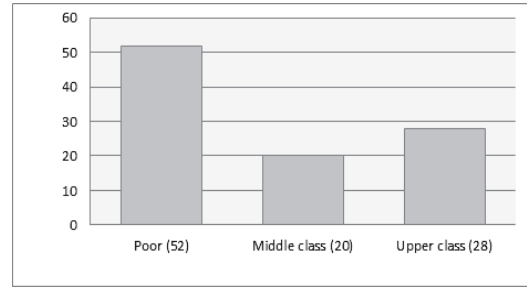
**Result & Observation:**

**Table I: Baseline characteristics of the study patients (n=100)**

Demography	Frequency	Percentage (%)
Age (years)		
15-25	18	18.0
26-35	43	43.0
36-45	39	39.0
Mean ± SD	29.57 ± 8.27	
Residence		
Rural	31	31.0
Urban	69	69.0
BMI (kg/m <sup>2</sup> )		
18.5-23.0	43	43.0
23.1-25.0	31	31.0
>25.0	26	26.0

In this study, maximum numbers of cases (43.0%) were between 26-35 years age group, mean age was 29.57 ± 8.27 years. Large numbers of respondents came from urban area (58%), followed by rural area (30%) and sub-urban/slum area (12%). Large numbers of respondents came from urban area (69.0%), followed by rural area (31%). Body mass index (BMI) shows that, 31.0% of patients were overweight and 26.0% detected as obese.

Figure- 1 shows socioeconomic status of the study population. Socioeconomically patients are grouped into three classes. Among the patients the poor class (52%) comprising the major percentage of the patients, which is followed by upper class (28%) and remaining are middle class (20%).



**Figure- 1: Socioeconomic status of the study population (n=100)**

Table II shows clinical manifestation of the respondents. Per vaginal bleeding was most common symptoms, present in 100% cases; next common symptoms were abdominal pain (76%), lump in lower abdomen(26%). Anaemia was the most common physical sign of AUB, present in 54% cases; followed by oedema 36%, abdominal mass 30%, ascities 18% and respiratory distress 18% cases.

**Table II: Clinical manifestation of the respondents (n=100)**

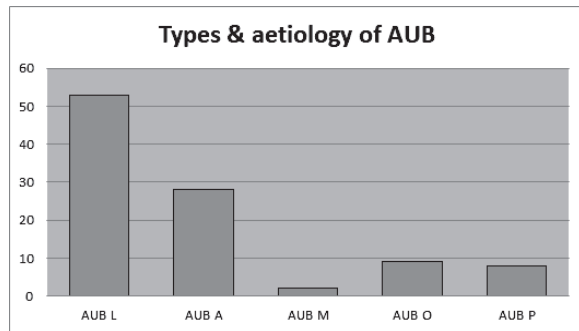
Clinical manifestation	Frequency	Percentage (%)
Clinical symptoms		
P/V bleeding	100	100.0
Lump in lower abdomen	26	26.0
Pain in the abdomen	76	76.0
Loss of appetite, dyspepsia	50	50.0
Nausea, vomiting	68	68.0
Physical sign		
Anemia	54	54.0
Oedema	36	36.0
Palpable abdominal mass	30	30.0
Ascities	18	18.0
Respiratory distress	18	18.0

Table III showing USG findings. Bulky uterus found in 75.0% cases, but normal endometrium was 94.0% subjects. Cystic ovary detected in 28.0% cases.

**Table III: Ultrasonogram findings (n=100)**

Ultrasonogram findings	Frequency	Percentage (%)	
Size of uterus	Bulky	75	75%
	Normal	25	25%
Endometrium	Hyperplasia	6	6%
	Atrophic	0	0%
Ovary	Normal	94	94%
	Cystic	28	28%
	Normal	72	72%

Figure 2 shows the types of Abnormal Uterine Bleeding. Maximum patient belongs to AUB-L (leiomyoma) group (53%) followed by AUB-A (adenomyosis) (28%); AUB-P (polyp) (8%); AUB-O (ovulatory) (9%) and AUB-M (malignancy) (2%).

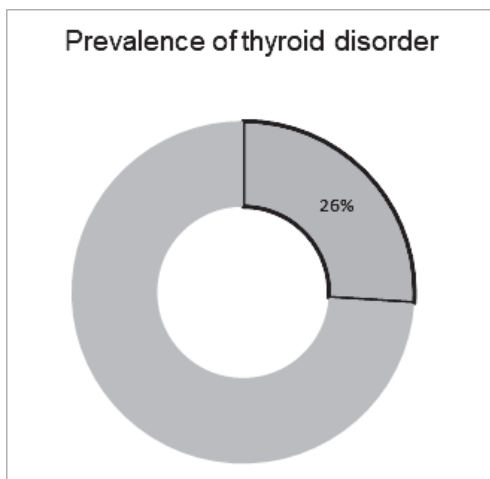


**Figure- 2: Types & aetiology of Abnormal Uterine Bleeding (n=100)**

**Table IV: Status of thyroid function tests among study subject (n=100)**

Thyroid status	Number of patients	Percentage (%)
Euthyroidism	74	74
Hyperthyroidism	8	8
Hypothyroidism	18	18

Present study demonstrated that, (74%) of patients of abnormal uterine bleeding were euthyroid state. Thyroid disorders were prevalent in 26% of AUB patients. The prevalence of Hypothyroidism was 18% and Hyperthyroidism was 8% among the AUB patients as assessed by the findings of their thyroid function tests.



**Figure-3: Prevalence of Thyroid disorders in AUB patients (n=100)**

Present study suggested that, prevalence of thyroid disorders was 26% in AUB patients in tertiary level hospital of Bangladesh. The prevalence of Hypothyroidism was 18% and Hyperthyroidism was 8% among the AUB patients as assessed by the findings of their thyroid function tests.

**Discussion:**

Abnormal uterine bleeding (AUB) is the commonest menstrual problem during perimenopause. In this study, the maximum numbers of cases (43.0%) were between 26-35 years age group. Mean age was  $29.57 \pm 8.27$  years. Large numbers of respondents came from urban area (69%). Per vaginal bleeding was most common symptoms, present in 100% cases; next common symptoms were abdominal pain (76%). On evaluation of types & causes of AUB, maximum patient belongs to AUB-L (leiomyoma) group (53%) followed by AUB-A (adenomyosis) (28%); AUB-P (polyp) (8%); AUB-O (ovulatory) (9%) and AUB-M (malignancy) (2%).

Epidemiological study reported that majority (97.46 %) of the women were less than 50 years of age, and most of the study population lived in urban area (59.7 %). Most women experienced symptoms of abnormal uterine bleeding for a period of 6 months to 1 year before seeking treatment (43.6 and 35.1 %, respectively).The most common presenting symptom in our study was heavy menstrual bleed (32.6 %) followed by intermenstrual heavy menstrual bleed in 28.3 % cases<sup>15</sup>.

The PALM and COEIN components accounted for 50.23 and 49.57 %, respectively. Leiomyoma (AUB-L) was assigned to be the major aetiology in 97/236 (41.1 %) in overall and 97/119 (81.51 %) in the structural group, whereas ovulatory disorders (AUB-O) were the proposed major contributor in the functional group accounting for 88/236 (37.28) of overall and 88/117 (75.27 %) of the later group cases<sup>15</sup>.

The PALM–COEIN classification has an advantage of consideration of the entire range of possible aetiologies but should be followed by further investigation to arrive at a more accurate and consistent diagnosis in perimenopausal group of women so as to rule out organic diseases particularly precancerous lesions and cancers. Chronic anovulation is a predominant phenomenon in perimenopause which is associated with an irregular and unpredictable pattern of bleeding that varies in amount, duration and character<sup>16</sup>. In our study the PALM and COEIN components contributed almost equally for AUB when assessed clinically with AUB-L being the major contributor in PALM group. Leiomyomas are known to be predominant in the age group presently studied.

Present study demonstrated that, (74%) of patients of abnormal uterine bleeding were euthyroid state. Thyroid disorders were prevalent in 26% of AUB patients. The prevalence of Hypothyroidism was 18% and Hyperthyroidism was 8% among the AUB patients as assessed by the findings of their thyroid function tests. Findings are consistent with other study.

The endocrine disturbances play a major role in the pathogenesis of abnormal uterine bleeding. The present study showed a significant association between women with

AUB and hypothyroidism. Result of this study is similar to the results of many previous studies<sup>13, 14</sup>. Whitaker et al., documented the hypothyroidism is one of the common diseases that must be assessed among women with abnormal uterine bleeding<sup>2</sup>. Thyroid disorders are common in females with subclinical hypothyroidism as it's the most common type<sup>14</sup>.

The mechanism by which the thyroid disorders is associated with AUB may be explained by altering thyroid-stimulating hormone (TSH) response, increasing prolactin levels, altering luteinizing hormone (LH) response, affecting peripheral conversion of androgens to estrogens, altering sex hormone-binding globulin (SHBG) and affecting coagulation pathways in addition to the effect on lipid profile. The hypothyroidism is a frequent cause of multiple disorders in women at reproductive age ranged from sexual dysfunction, menstrual abnormalities, and infertility<sup>17</sup>.

Menstrual irregularities are seen in both hyperthyroidism as well as hypothyroidism. Previous study showed that hypothyroidism constitutes 11% of women with AUB and hyperthyroidism did present in 1% of them<sup>14</sup>. These findings are a little higher than the results of previous Iraqi study conducted by Al-Hakeim which found that among women with menstrual disturbances, hypothyroidism present in 16.1% of them and hyperthyroidism was present in 3.4% of them<sup>18</sup>. This difference in thyroid dysfunction between two studies might be due to geographical variation and high prevalence of thyroid disorders in subcontinent.

#### Conclusions:

Thyroid dysfunction is a common cause of abnormal uterine bleeding among reproductive-age women. Prevalence of hypothyroidism (18%) was more common than hyperthyroidism (8%) in AUB cases. It can be concluded that thyroid dysfunction is associated with menstrual disturbances (abnormal uterine bleeding) which get relieved with the correction of thyroid dysfunction, so thyroid assessment by thyroid function tests should be performed in all patients with menstrual irregularities to avoid unnecessary interventions like hormone replacement and surgery.

**Conflict of Interest:** None.

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