EVALUATION & WORK UP OF A WOMAN WITH MENORRHAGIA

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***Abstract** : Menorrhagia is defined as heavy cyclical bleeding occurring at normal intervals with bleeding increased either in amount (> 80 ml) or duration (>7 days). A detailed history and examination can help the clinician make a fairly accurate probable diagnosis. Further investigations to confirm the diagnosis are guided by factors like age of the woman, presence or absence of high risk factors for endometrial carcinoma and by presence of indicators of any underlying abnormality. The first step is to rule out pregnancy and assess for severity and type of anemia by a detailed blood count and peripheral smear. Depending on the history, bleeding disorders and other medical disorders like hypothyroidism and PCOS should be investigated. As far as use of various diagnostic procedures for evaluation of endometrium is concerned, TVS appears to be a logical first choice as it is simple, non-invasive and cost-effective and helps in deciding the next step in work up of menorrhagia. If a focal lesion is suspected on TVS, SIS or hysteroscopy directed biopsy is indicated and if a diffuse lesion is suspected then an office endometrial biopsy may suffice.*

INTRODUCTION

Normal menstruation refers to cyclical flow of blood lasting for 2-7 days at an interval of 28 ± 7 days. The average blood loss is 40 ± 20 ml. per cycle[1]. Abnormal uterine bleeding (AUB) is defined as changes in frequency of menses, duration of flow or amount of blood loss. It encompasses both cyclical and non cyclical bleeding. The incidence varies from 10-30% of women in the reproductive age group and up to 50 % of peri-menopausal women[2].

Menorrhagia is defined as heavy cyclical bleeding occurring at normal intervals with bleeding increased either in amount (> 80 ml) or duration (>7 days). Even a single episode of prolonged bleeding lasting for more than 7 days can be classified as menorrhagia[3]. When the bleeding is prolonged as well as irregular it is known as menometrorrhagia. Population studies have shown that almost 9-14 % of women have blood loss averaging more than 80 ml per cycle[5].

It has been shown that patients' perception of increased blood loss may not actually be true specially so in adolescents due to their limited knowledge of what is normal. The commonest subjective method to ascertain the amount of blood loss is a detailed menstrual history as regards the number and type of pads used by the woman and any history of passage of clots. Another method to ascertain whether the woman has excessive menstrual loss is to estimate the hemoglobin concentration. Women with menorrhagia are more likely to have hemoglobin less than 12 gm %. Estimation of serum Ferritin levels (normal 50 – 150 mgm/dl) is a better predictor. It has been shown to correctly predict 60 % of women with > 80 ml blood loss during their periods [5].

An objective pictoral method for assessing blood loss was proposed by Higham (1990). The woman is asked to observe the degree of soakage of each pad she uses and mark it on a chart provided to her. Scores are assigned depending on the degree of soakage.

Score 1 – lightly stained pad
Score 5 – moderately soaked pad
Score 20 – completely soaked pad
Score 1 – passage of small clot
Score 5 – passage of large clot

The total score per cycle is calculated and if it is more than 100 then it implies that the menstrual blood loss of the woman per cycle is > 80 ml.

At a cut off of 100, this method has a sensitivity of 86% and specificity of 89 %[6].

AETIOLOGY OF MENORRHAGIA

The aetiology of menorrhagia can be broadly classified into four categories (Table No 1) hormonal, haematological abnormalities, genital organ or genital tract related pathology and idiopathic (DUB) [9, 10]. However the contribution of each of these four categories to menorrhagia varies according to the age of the woman. The commonest cause in adolescent girls is hormonal imbalance compared to genital tract related pathology in young adult women and premalignant and malignant lesions in peri and postmenopausal women.

***Table1:** Etiology of Menoehagia*

Hormonal	Bleeding disorders	Genital tract and genital organ related pathology	Idiopathic
• Immature hypothalamus-pituitary-ovarian axis. • Hypothyroidism • Polycystic ovarian syndrome • Hyperprolactinemia	Congenital • von Willibrand disease • Idiopathic thrombocytopenic purpura **Acquired** **Drug induced** • Anticoagulants as in case of heart disease • Antineoplastic drugs for malignancies **Malignancies** • Leukaemia	• PID (Tubercular, Chlamydia) • Fibroid • Adenomyosis • Endometrial polyps • Endomerial cancer • Oestrogen producing ovarian tumours • Use of IUCD	• DUB

WORK UP A WOMAN PRESENTING WITH MENORRHAGIA

Every woman presenting with menorrhagia needs to be systematically worked up. A detailed history is important as a good history can help the clinician to make a provisional diagnosis which can be further fine tuned by examination and finally confirmed by investigations.

History

History should broadly include a detailed menstrual history, sexual

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history, medical history, history of drug intake and history of any bleeding disorders.

Menstrual history:

The menstrual history should include the age at menarche, duration of symptoms, and whether symptoms are progressive or not. Details of previous and present menstrual cycles as regards the frequency, duration and blood flow should be recorded. Any history of dysmenorrhoea should be elicited as it helps in making the differential diagnosis of menorrhagia. In case dysmenorrhoea is present, history related to the type of dysmenorrhoea needs to be asked. Dysmenorrhoea is congestive if the pain starts before the periods and gets relieved within a few hours of onset. This type of dysmenorrhoea is usually seen in women with P.I.D. or fibroids. It is as a result of pelvic congestion. Dysmenorrhoea which starts with the onset of periods is spasmodic and gets relieved in a day or so is spasmodic dysmenorrhoea. It is seen in women with fibroids, specially submucous or intramural wherein the uterus tries to expel the fibroid during periods resulting in spasmodic dysmenorrhoea. The patient typically describes the pain as that similar to labour pain. In adenomyosis the dysmenorrhoea starts before the periods, increases throughout the period and persists even after the periods. This type of secondary dysmenorrhoea in a perimenopausal woman is typical of adenomyosis. History of severe dysmenorrhoea with menorrhagia is strongly suggestive of adenomyosis or a submucous fibroid or fibroid polyp.

The date of the last menstrual period is important. It not only helps to rule out pregnancy but also helps in planning endometrial biopsy in the premenstrual phase. It is also important to know if the last period was normal in flow or not. This is because a woman may be pregnant and has implantation bleeding in the form of scanty periods but later presents with heavy bleeding with dysmenorrhoea which is actually inevitable or incomplete abortion. Sometimes women with anovulatory cycles may have very less bleeding in one cycle followed by very heavy flow in the next cycle.

Sexual history:

One should ask if the woman is sexually active and whether she has ever had any sexually transmitted disease.

Medical history:

Symptoms associated with medical conditions resulting in anovulation in self or her family members should be inquired. Table no. 2 gives the symptoms specific to the medical conditions.

Table 2: *Clinical presentation - Etiology-wise*

Symptoms	Associated medical condition
Acne , hirsutism, weight gain, infertility, acanthosis nigricans , type 2 diabetes mellitus	Polycystic ovarian syndrome (PCOS)
Any increase or decrease in weight, cold or heat intolerance	Thyroid disorder
Headache , blurring of vision, galactorrhoea	Pituitary tumours

History of drug intake:

History of use of anticoagulants like warfarin or asprin, chemotherapeutic agents, illicit herbs ,dietary supplements, if present, could be a cause of menorrhagia. History of IUCD insertion is important as it is associated with menorrhagia in the initial 3-6 cycles.

Bleeding manifestations:

History of any cutaneous or mucosal bleeding, easy bruisability, childhood epistaxis, excessive bleeding from superficial cuts and scratches, prolonged bleeding during dental extraction or history of postpartum haemorrhage could be due to an underlying bleeding disorder. In severe forms these disorders could also present with hemarthrosis and dissecting intramuscular haematomas. History of blood or blood component therapy should always be elicited.

Clinical examination:

This should include the following

·(1) Pulse and blood pressure; (2) Pallor; (3) Icterus; (4) Palpable lymph nodes; (5) Sign of PCOS or androgen excess, thyroid nodule or enlargement, galactorrhea; (6) Bruising and petechiae; (7) Abdominal examination for any palpable lump, liver and spleen; (8) Per speculum and per vaginum examination to detect the possibility of pregnancy, foreign body or an anatomic source of bleeding. A bimanual examination may elicit tenderness suggestive of PID; an adnexal mass consistent with a functioning ovarian neoplasm, ectopic pregnancy, Tubo-ovarian mass or cyst; or uterine enlargement associated with pregnancy, fibroids, endometriosis or malignancy; (9) Pelvic examination is avoided in adolescents who are not sexually active. A per rectal examination may be carried out instead. Examination under anaesthesia can be done in those adolescents who do not respond to medical therapy.

Investigations:

A detailed clinical evaluation should be followed by investigations.

1) Urine *pregnancy test* to rule out pregnancy.
2) *Cervical cytology* in sexually active women if not done in the last three years.
3) Complete *blood count* with peripheral smear for degree of anaemia, type of anaemia and any evidence of thrombocytopenia
4) ESR
5) *Reticulocyte count* - if raised helps to confirm a history of excessive bleeding in patients who have a normal haemoglobin level
6) Serum *ferritin* levels
7) *Liver function tests*
8) *Chest X- ray*
9) In the presence of signs and symptoms of *endocrinal disease*, following tests should be carried out
   - *Thyroid disease*- SerumT3, T4, TSH
   - *Galactorrhe*a- Serum Prolactin
   - *Hyperandrogenism*- S.Testosterone, S. Dehydroepiandrostenedione sulfate, S.17 OH Progesterone
   - *PCOS*- Day2 FSH and LH, 2hr GTT and serum insulin and sex hormone binding globulin.
10) *Ultrasonography* – A transabdominal ultrasound examination followed by transvaginal ultrasonography is a simple, inexpensive and non invasive method for evaluation of the endometrium and adnexa in cases of menorrhagia. It can be used as an initial investigation to select cases which will require further evaluation by saline infusion sonohysterography (SIS), hysteroscopy or endometrial biopsy. The initial scan can rule out pregnancy and other anatomical abnormalities like polyps (sensitivity 65.2% – 72% , specificity 87.9% - 92 %) and fibroids (sensitivity 95% - 95.8 % , specificity 92% – 95.5%) [11,12]. When done on day 4-6 of the menstrual cycle a cut off of 5 mm is used to rule out any significant endometrial pathology [13-16]. Women with

thicker endometrium can then be evaluated by saline infusion sonography. SIS involves ultrasound visualization of the endometrium after infusion of 5-10 ml of sterile saline and helps in distinguishing between globally thickened endometrium and focal abnormalities (sensitivity - 91%-94% , specificity 93% -98.7%) [11,12] .Where the endometrium is globally thickened (> 3mm single layer) one can conduct a directed endometrial biopsy. Combining SIS with directed biopsy results in a sensitivity of 95%-97 % and specificity of 70%-98 % for endometrial pathology. [17,18]. Presence of cystic ovaries support the diagnosis of DUB (anovulatory) or PCOS, whereas a unilateral adnexal mass may be suggestive of an ovarian tumour.

11) **Endometrial sampling-** It should be done in all women over 40 years and in younger women with high risk factors for endometrial cancer. It is also indicated in women who have no improvement in symptoms after 3 months of medical management. It is rarely indicated in adolescents. The sample should be sent for histopathological examination and AFB smear and culture. In perimenopausal women it should be coupled with endocervical sampling.

Risk factors for endometrial carcinoma

- Age > 40 years
- Weight > 90 kgs.
- History of anovulatory cycles
- Nulliparity with or without history of infertility
- History of use of tamoxifen
- Presence of diabetes / hypertension
- Family history of endometrial / colon cancer

Techniques of endometrial sampling

The various options available to a clinician for endometrial sampling are:

(i) Office endometrial biopsy – Office endometrial biopsy has a sensitivity of 67%-96% [19-21] but may miss upto 18 % of focal lesions [22]. It can be performed with the help of a Karman's cannula no. 4 and a 20 cc syringe with which required negative pressure is created or a pipelle's curette and does not require any cervical dilatation. As compared to dilatation and curettage it is a relatively safer technique with less chances of hemorrhage, infection and perforation.

(ii) Dilatation and curettage – Requires anaesthesia and has no major advantage over office biopsy. However in post menopausal women, Fractional curettage should be a preferred technique of endometrial sampling for ruling out endometrial carcinoma.

(iii) Hysteroscopy directed biopsy – Besides evaluation of the endometrium, hysteroscopy also has the advantage of diagnosing focal lesions like polyps, submucous fibroids and focal endometrial carcinoma.

8) Evaluation of haematological disorder: This is indicated in adolescent girls presenting with menorrhagia or when there is a clinical suspicion of a coagulopathy.

Routine use of screening tests like bleeding time, platelet count, PT, aPTTK is useful as it saves time and helps to direct the course of further investigations.

i) Bleeding time - It adds to the diagnosis if prolonged but otherwise may have little clinical use in diagnosis and

Table 3*: Stepwise approach for evaluation of abnormal aPTTK and/or PT* [23,24]

Step I: Prolonged aPTTK and /or PT → Review history to rule out drug intake (heparin, warfarin), Liver disease etc

Step II: If negative history

Assess factor VIII levels → normal/reduced

Step III: (a) If factor VIII reduced → *Tests for confirming vWD

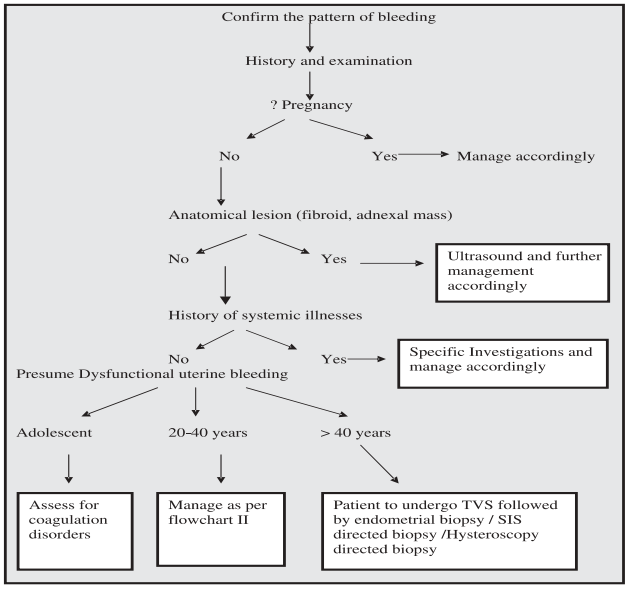
Abnormal (vWD) | Normal Haemophilia A

*von Willibrand disease[23, 24]:

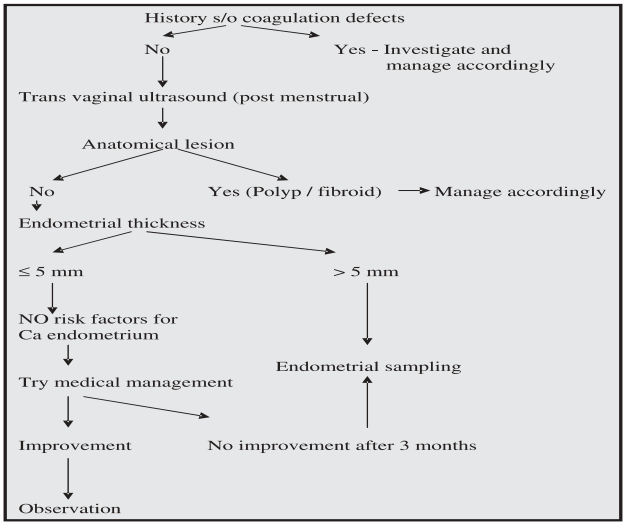
Tests include assays for von Willebrand factor activity (ristocetin cofactor), vWF antigen and a vWF multimer analysis and / or low-dose ristocetin aggregation assay if required.

(b) If factor VIII level normal → assess factor IX → decreased (Haemophilia B)

Flow Chart I: *Algorithm of work up of a woman with menorrhagia*



Flowchart II: *Further work up in 20-40 years old women with menorrhagia*



management. Normal bleeding time is 2 to 6 minutes.

ii) Platelet count- It provide the most reliable and reproducible test of primary haemostasis. A low platelet count should be verified by a repeat platelet count and adequacy of platelets on peripheral smear.

iii) Prothrombin Time (PT) and activated Partial Thromboplastin Time (aPTTK)

PT- It assesses the extrinsic and common pathway (factor VII, factor V, X, prothrombin, fibrinogen.)

aPPTK- It measures all the coagulation factors involved in the intrinsic and common pathways (factor VIII, IX, XII, factor V, X, prothrombin, fibrinogen). It has been accepted as the best single test for coagulation disorders. It reflects reduced levels of factor VIII and vWF.

The above tests provide a presumptive diagnosis, which can be further verified by the confirmatory methods.

An algorithm of work up of a woman with menorrhagia is shown in flowcharts I and II. The investigative work up of a patient of menorrhagia is essentially guided by the age of the woman, history, presence or absence of high risk factors for endometrial carcinoma and clinical examination. TVS appears to be a logical first choice as it is simple, non-invasive and cost-effective and it helps in deciding the next step in work up of menorrhagia. If a focal lesion is suspected on TVS, SIS or hysteroscopy directed biopsy is indicated and if a diffuse lesion is suspected then an office endometrial biopsy may suffice.

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