

## Evaluation of etiological factors and management of puberty menorrhagia

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### Abstract

**Objectives:** To evaluate the causes of puberty menorrhagia and effect of hormonal (Progestogens, estrogens and Combined Oral Contraceptive pills) and non-hormonal methods in the management of puberty menorrhagia.

**Methods:** This prospective study included 51 subjects, who presented with puberty menorrhagia to Department of Obstetrics and Gynaecology, King George's Medical University, Lucknow from August 2014 to August 2015. Assessment of each case with thorough history, physical examination and laboratory investigations was done. The underlying cause was diagnosed and the relevant treatment started and subjects kept under regular follow up.

**Results:** In 26 (50.98%) subjects, immaturity of hypothalamic pituitary ovarian axis was the main cause of puberty menorrhagia, 6 (11.76%) subjects had hypothyroidism, 5 (9.80%) subjects had polycystic ovarian syndrome, 4 (7.8%) subjects had idiopathic thrombocytopenic purpura, 2 (3.9%) subjects had disseminated intravascular coagulopathy, 3 (5.88%) subjects had hyperprolactinemia, 3 (5.88%) subjects had both hypothyroidism and hyperprolactinemia, 2(3.92%) subjects had fibroid uterus. All patients responded to medical management.

**Conclusion:** Puberty menorrhagia is a distressing condition both for the subject as well as her parents. Most of the cases are due to ovulatory cycles which are a self-limiting condition at perimenarchal age group. Counseling and reassurance of the subjects is an important part of management. Long term medical treatment is successful in the majority of cases and rarely surgical intervention is required. Blood transfusion is required in a few cases.

**Keywords:** Puberty, Menorrhagia, Causes, Management.

### 1. Introduction

Puberty is defined as a period during which secondary sexual characters begin to develop and the capability of sexual reproduction is attained. It is the process of biological, cognitive and psychosocial maturation [1,2] Puberty menorrhagia is a very common gynaecological problem in adolescents, incidence being 10% in Indian population. Puberty menorrhagia is defined as excessive bleeding more than 80 ml or more than 7 days between menarche and age 19 year [3]. The onset of menstruation is affected by a number of factors: genetics, nutrition, body weight and maturation of the hypothalamic pituitary ovarian axis. A normal menstrual cycle lasts from 21 days to 35 days with 2-6 days of flow and an average

blood loss of 20 – 60 ml. The upper limit of blood loss being 80 ml. During the first 2-5 years after menarche, most cycles are an ovulatory. However the cycles are somewhat regular, within a range of approximately 21 to 45 days, in contrast to adult women whose cycle typically ranges between 21 to 38 days. One fourth of girls present with a pattern of  $\pm 10$  days and a cycle length of 21- 45 days are established within first 3 cycles; in half of girls by 7<sup>th</sup> cycle and in 2/3<sup>rd</sup> of girls it is established after 2 years of menarche[1]. The mean duration of menses is 4.7 days; 89% of cycles last 7 days. In per cycle 35 ml average blood is loss, and the major component of menstrual discharge is endometrial tissue [4]. The transition of an ovulatory to ovulatory cycles during adolescence takes place during the

first several years after menarche. Majority of the patients will return to regular menstrual pattern by 3-4 years after menarche [5]. The younger the age at menarche, sooner regular ovulation is established. Puberty menorrhagia in adolescent age group is almost always caused by an ovulatory cycles due to immaturity of hypothalamo - pituitary ovarian axis. This problem range from minor deviation from the average menstrual patterns to life threatening menarche [6,7]. If an ovulation persists for longer than 4 years, the girl has a tendency for obesity and she will have high chance of developing PCOD and infertility. These patients also have an increased risk of getting adenocarcinoma of endometrium in later year [5]. Most common causes of puberty menorrhagia is an ovulation (94%), other causes (26%) are thyroid disorder (12-15 %), hematological disorders, ITP, Von-Willebrand disease, Factor XI deficiency etc), PCOS (5-10 %), infections etc.

The seriousness of symptoms is usually a subject of great concern for both patient and the parents and thus deserves attentive consideration. Therefore we aim to investigate the various etiological factors and management of puberty menorrhagia as recognition of the underlying cause and timely management can be lifesaving.

## 2. Material and Methods

In this Prospective study total 51 young girls from age of menarche to 19 years recruited after taking informed consent with history of excessive bleeding pervaginum, attending outpatient department (OPD) or admitted to the Department of Obstetrics and Gynaecology, King George's Medical University, Lucknow were included in the study. The study was carried out from August 2014 to August 2015. Excessive blood loss during menstruation was considered if the more than seven days menstruation /or history of passage of clots. A detailed history regarding age of patient, age of menarche, previous menstrual history was taken. The presenting complaints about onset, duration and amount of blood loss were noted. Blood Requirement, component therapy and response to previous therapy were also recorded. The medical history included history of recent weight change, tuberculosis, thyroid disorders and haematological disorders (excessive bleeding was noted. Personal history included history of any drug intake. Family history such as tuberculosis, thyroid disease and bleeding diathesis were also recorded. Pallor, lymphadenopathy and gum bleeding of patients were observed. The pulse and blood pressure were recorded. Abdominal palpation was done for hepatosplenomegaly and abdominal masses. Tenderness in sternum and other bony areas and joint swelling was looked. Skin was examined for any purpuric spots, acne, hirsutism and features of hyperandrogenism. A protocol of investigation was made. The base line investigations were done including Pelvic ultrasound for

uterine and ovarian morphology. Some investigations (Von Willebrand factor activity, Ristocetin cofactor assay, 21 day serum progesterone level) were done in selected patients.

The management protocol depended upon the condition of the patient and the underlying cause of menorrhagia. In hemodynamically stable an ovulatory bleeding patient, mefenamic acid, tranexamic acid and antifibrinolytic prostaglandin synthetase inhibitors were used as first line therapy during the days of menstruation for control of blood loss. Hormones such as progestins, oral contraceptive pills were prescribed in cases not responding to non-hormonal therapy. Anaemia was corrected by oral hematinics or blood transfusion / component therapy in consultation with a haematologist. For correction of hematological disease and thyroid disease, the specific treatment was carried out. Girls above 20 years of age and women with pregnancy related bleeding were excluded in this study.

### 2.1 Statistical analysis

The statistical analysis was done using SPSS version 15.0 statistical analysis software. The value were represent in number percentage (%) and mean  $\pm$  SD. ANOVA tests was used to compare within group and between group variance amongst the study group. To test the significance of two means the student "t" test was done.

## 3. Result

In this study most of the subjects were of 14-16 years of age group (45.09%) and 21(41.17%) were above 16 years. Most of the subjects 35.29% belong to lower middle class and literacy rate observed as 96%. The symptom with puberty menorrhagia remained up to one year in 25 subjects 49.01% (Table -1), 18 subjects (35%) had duration of symptoms for >6 months but less than 1 year and only 8 subjects had for <6 months (Table-1). According to transabdominal ultrasonography (USG) findings 86.27% subjects found with menorrhagia no abnormal findings, 3.92% were found to have Fibroid in Uterus and 9.8% were diagnosed to have PCO (Table1). In this present study 37.25% subjects were severely anemic i.e. hemoglobin % (<8gm %) and required immediate admission and blood transfusion.

Among 51 subjects presenting as puberty menorrhagia, 50.98% subjects the cause of puberty menorrhagia was an ovulatory cycles due to immature H-P-O axis. 11.76% had isolated hypothyroidism while 5.88% had hypothyroidism along with hyperleptinemia, 11.76% were diagnosed to have hematological disease (ITP & DIC) 9.80% subjects were diagnosed as PCOD and 3.92% fibroid uterus was found (Table 2).

Table 3 show that 23 subjects hematinics were combined with specific non hormonal treatment as per underlying cause, 5.88% subjects responded to reassurance, hematinics and tranexamic acid only, tab thyroxin was

given in 17.64% subjects, tab-Cabergoline was given in 11.76%, tab Metformin was given in 9.8% subjects (Table 4). 28 out of 51 subjects who were treated with hormonal therapy, all 14 patients 100% responded well to

progesterone alone, 4 out of 8 (50%) responded to progesterone f/b combined oral contraceptives, 3 out of 6 (50%) responded to combined oral contraceptives (COCs) (Table 5).

**Table 1: Distribution of Age, Duration of Symptom, and USG Finding (n=51)**

	No. of subjects (n=51)	Percentage (%)
<b>Age (years)</b>		
<14	7	13.72%
14-16	23	45.09%
17-19	21	41.17%
<b>According to Duration of Symptoms</b>		
Less than 6 months	8	15.68%
≥ 6 months to < 1 years	18	35.29%
≥1 years	25	49.01%
<b>According to USG Finding</b>		
Normal finding	44	86.27%
Fibroid in Uterus	2	3.92%
<b>Polycystic ovaries (PCO)</b>	5	9.80%

**Table 2: Distribution of Subjects According to Etiological Factors (n=51)**

Etiological factors	No. of subjects (n=51)	Percentage (%)
An ovulatory Dysfunctional Uterine Bleeding	26	50.98
Hypothyroidism	6	11.76
Hematological cause	6	11.76
Idiopathic Thrombocytopenic Purpura (ITP)	4	
Disseminated Intravascular Coagulopathy (DIC)	2	
Hyperprolactinemia	3	5.88
Both Hypothyroidism & Hyperprolactinemia	3	5.88
Fibroid uterus	2	3.92
PCOD	5	9.80

**Table 3: Distribution of subjects according to treatment Modalities (n=51)**

Treatment Modalities	No. of subjects	Percentage (%)
Reassurance +Hematinics + Tranexemic acid	3	5.88%
Hormonal therapy	28	54.89%
Non-Hormonal therapy	20	39.21%

**Table 4: Non- Hormonal Management (n=23)**

Drugs given along with hormonal treatment	No. of subjects	Percentage (%)
Hematinics +Tranexamic acid only	3	5.88
Hematinics + Tranexamic acid f/b hormones	11	21.56
Hematinics +Thyroxine	9	17.64
Hematinics+Dopamine receptor agonist (Cabergoline)	6	11.76
Hematinics+Metformin	5	9.8

**Table 5: Hormonal Management (n=28)**

Hormones used	No. of subjects (n=32)	Percentage (%)
Progesterone only	14	27.45
Progesterone followed by Combined Oral Contraceptive pills (COC)	8	15.68
Combined Oral Contraceptive Pills (COC) only	6	11.76

#### 4. Discussion

Menarche is a hallmark incident in the life of adolescent girls. It is the process of cognitive, psychosocial, and biological maturation. Puberty menorrhagia is defined as uncontrolled bleeding in 19 years of age [8]. During puberty, maturation of the hypothalamic pituitary ovarian axis is characterized by an increase in frequency and

amplitude of pulsatile GnRH, which initiates and regulates secretion of pituitary gonadotrophins [3,4]. During prepubertal years LH is secreted primarily at night in an episodic fashion. With the progression to puberty, day LH peak increases in a pattern similar to that seen at night. The timing of these LH pulses is crucial in establishing normal ovulatory cycles. Increase in basal LH as well as immature

timing of pulses results in ovulatory cycles. These cycles are characterized by levels of LH and FSH secretion that are sufficient to induce follicular development and oestrogen production but inadequate to induce follicular maturation and ovulation. Thus unopposed oestrogen stimulates endometrial growth. This ultimately outgrows its blood supply and architectural support, resulting in partial breakdown and shedding in an irregular manner [9]. In proliferative phase, the endometrium synthesizes equal amounts of PGF2 (vasoconstrictor and weak platelet aggregator) and PGE2 (vasodilator and weak platelet antiaggregator). However in the luteal phase the level of PGF2 progressively increases under the influence of oestrogen and progesterone. In normal menstruation, the ratio of PGF2: PGE2 is 2:1 so that it is the vasoconstrictor and platelet aggregator action that predominates. In an ovulatory DUB the lack of progesterone results in decreased PGF2: PGE2 ratio and relative increase in vasodilator PGE2 which could account for increased mean menstrual blood loss. It could also account for absence of uterine contractions. This can be a recurrent problem until the cycle becomes regular. Occasionally anemia results with a haemoglobin level as low as 6 or 7 gm/dl [10].

In this study 13.72% belonged to early adolescence group, 45.09% to middle adolescence and 41.17% were belong from late adolescence period. This study is comparable with that of Gautam *et al* [11], who found similar distribution of subjects in different age group. This study show that majority of the subjects (39.21%) presented as menorrhagia i.e., heavy menstrual bleeding in regular cycle, 29.41% subjects presented as oligomenorrhagia i.e. prolonged cycles with heavy menses, 25.49% presented as polymenorrhagia i.e. short cycle with heavy menstrual flow and only 5.88% subjects had a complain of intermenstrual heavy bleeding.

In this study, an ovulatory dysfunctional uterine bleeding due to immature hypothalamo-pituitary-ovarian (HPO) axis was found to be the predominant underlying etiology of puberty menorrhagia constituting ~51% were as Chowdhary *et al* [12] reported 60%, Khosla *et al* [13] reported 60%, Joshi *et al* [2] reported 78% and Shanti Sri *et al* [14] 58.3% cases of puberty menorrhagia due to immature hypothalamo-pituitary-ovarian axis. In this study hypothyroidism was found to be the cause in ~18% followed by ~12% Hyperprolactinemia, hematological disorder ~12% (ITP+DIP), ~4% Fibroid uterus and ~10% PCOD whereas pervious study found an ovulatory bleeding ~60%, hypothyroidism ~10%, hematological disorder ~15%, fibroid uterus ~3% & PCOD ~3% [15], Shanti Sri *et al* [14] found that out of 48 patients, 28 patients had immaturity of the HPO axis as they had a normal USG and hormonal assays. 10 were PCOD, 4 were positive for tuberculosis, 3 patients had elevated serum TSH levels and 2 patients had fibroid uterus [14].

Treatment is directed towards menstrual regulation and treating the hormonal alterations. It includes counseling and reassurance. First line treatment in mild cases is tranexamic acid and NSAIDs during the menstrual cycle [16]. Tranexamic acid is effective, safe, the bioavailability is 35% which requires administration of at least 1 gm 4-6 hourly [17]. Hormonal treatment is required where the girl is anemic or where the problems is repeating and confine her activity for 3-6 months. Progesterones alone are generally effective but can be used in combination with estrogen. This similar response that conducted by Khan *et al* [17] and Davey *et al* [18] who concluded similar response to treatment with progesterone. Progesterone can be used as -Cyclic medroxy progesterone acetate (MPA) 5-10 mg per day for 10-13 days per month for 1 or 2 months OR Tab. MPA 10 mg from day 5-25 for 3-6 months. Progesterone followed by COCs can be used as norethisterone 20-30 mg in divided doses for 24-48 hours for initial control of bleeding then the dose was gradually tapered to 10 mg once daily for remaining length of cycle (21 days). Following the withdrawal bleeding combined oral contraceptive pills were started from the D5 of withdrawal flow and continued for 21 days for 3 cycles. Patel *et al* [19], also used similar regimen of hormonal therapy in his study. In patients with severe bleeding associated with hemodynamic changes blood transfusions are indicated with administration of intravenous conjugated equine estrogen, 25 mg I/V every 4 hours for up to 24 hours. Within 24 hours bleeding usually decreases and then oral estrogen can be substituted. Progesterone was also usually added this similar result also found by Devore *et al* [20]. Previous study show that Young girls with blood coagulopathies are at a high risk of abnormal bleeding with the onset of menarche, bleeding is usually heavy causing anemia and may require blood transfusion and found 20% of cases of menorrhagia to be due to primary coagulation disorders [21]. In our study 6 (11.76%) patients had coagulation defects. Platelet function defects are an important cause of menorrhagia [22].

In our study 4 patients (7.8%) had idiopathic thrombocytopenic purpura. Phillip *et al* [23] reported that 3 patients (8.6%) had idiopathic thrombocytopenic purpura. Acute idiopathic thrombocytopenic purpura is most commonly seen in the young and is immunological, caused by immune complex containing viral antigens that bind to platelet Fc receptors or by antibodies produced against viral antigens that cross react with platelets. The majority of studies in the west report von Willebrand disease as the most common inherited bleeding disorder leading to menorrhagia whereas studies in South East Asia have found platelet function disorders as the leading inherited bleeding disorder in women with menorrhagia [24]. Present study concluded that Endocrine disorders can cause an ovulation producing an environment of unopposed oestrogen. In the

absence of progesterone, the endometrium eventually breaks down causing menorrhagia. The menorrhagia associated with hypothyroidism responds to thyroid replacement therapy in doses sufficient to correct the other manifestations of the condition.

## 5. Conclusion

So, the primary cause of puberty menorrhagia was found to be an ovulatory cycles due to underlying immature hypothalamo-pituitary-ovarian axis and hormonal therapy mainly progesterone was found to be the main stay in regularizing the menstrual cycle. However role of counseling, reassurance and hematinics cannot be underrated. Bleeding disorders are another. Assessment of each case with thorough history, physical examination, and laboratory investigations are crucial in reaching the diagnosis. Once a proper diagnosis is made, counseling of the patient and her parents, follow up and long term therapy and blood transfusion is required in some cases.

**Conflict of interest:** The author (s) confirms that this article content has no conflict of interest.

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