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Original Research Article

Etiological Factors and Management of Puberty Menorrhagia in a Rural Medical College of South Bengal: A Prospective Study

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ABSTRACT

Introduction: One fourth of the population in developing countries comprises girls below 20 years of age and abnormal uterine bleeding accounts for approximately 50% of all gynaecological visits among the adolescent girls. There are very few studies on puberty menorrhagia in this subcontinent and all the studies have very few numbers of subject. The aim of this study is to find out causes of puberty menorrhagia and role of medical and operative management in a rural medical college of South Bengal.

Materials and methods: After ethical committee approval and informed patient consent 200 young girls either attending outpatient department or admitted in the indoor with history of excessive bleeding per vagina between menarche and 19 yrs of age were included in the present study. After proper history, physical examination and investigations as appropriate the cause of excessive bleeding was diagnosed and treated accordingly.

Results and Observations: Most (67%) of the patients had puberty menorrhagia for 6 months to 1 year and 63.5% of all patients had hemoglobin level 10 gm % or less. Anovulatory dysfunctional uterine bleeding (72.0%) and polycystic ovarian disease (10.5%) were the two main etiological factors responsible for puberty menorrhagia in our study. Hypothyroidism (8.5%), idiopathic thrombocytopenic purpura (3%) and genital tuberculosis (2.5%) were other causes of excessive uterine bleeding in the present study.

Conclusion: Commonest cause of puberty menorrhagia is immaturity of the hypothalamic - pituitary ovarian axis resulting in anovulation. Proper evaluation by history, clinical examination and investigations are important to diagnose the etiology of puberty menorrhagia. Most of the cases respond well with medical therapy.

Key Words: Puberty, Menorrhagia, Causes, Management.

INTRODUCTION

The term puberty refers to the whole period of time during which secondary sexual characteristics develop, menstruation begins in females and psychosexual outlook of a human being changes. [1] There are five main physical features of puberty in female: breast growth, pubic hair growth, axillary hair growth, increase in height and onset of menstruation (menarche). Puberty menorrhagia is defined as excessive

bleeding in amount (>80ml) or in duration (>7days) between menarche and 19 years of age. [2] The onset of menstruation does not mean that ovulation has occurred; in majority of the cases early menstrual cycles are anovulatory. Without ovulation unopposed estrogen results in endometrial proliferation, with eventual excessive menstrual bleeding. The cycle length also varies for several years after menarche. It may take about 5-8 years before normal menstrual cycle is established. During this time adolescent girls usually present with menstrual irregularities. [3]

One fourth of the population in developing countries comprises girls below 20 years and in India, children under 15 years of age constitute about 40% of the population. [4,5] It is also reported that abnormal uterine bleeding accounts for approximately 50% of gynaecological visits in adolescent girls. [6] Thus in our country, puberty menorrhagia is a common gynaecological disorder leading to both morbidity and sometimes mortality in adolescent girls. There are very few studies on puberty menorrhagia in this subcontinent and all the studies have very few numbers of subject.

The aim of this study is to find out causes of puberty menorrhagia and role of medical and operative management in a rural medical college of South Bengal.

MATERIALS AND METHODS

After ethical committee approval and informed patient consent 200 young girls either attending outpatient department or admitted in the indoor with history of excessive bleeding per vagina between menarche and 19 yrs of age were included in the present study. The study was carried out from 1st January 2010 to 31st December 2014 in the department of Gynecology at a rural medical college of South Bengal.

Blood loss during menstruation was considered excessive if the patient had prolonged cycle >7 days and/or there was history of passage of clots and were included in the study. Those patients with history of trauma or pregnancy test positive were excluded from the study.

A detail history regarding age, socioeconomic status, milestones of growth and onset of puberty were taken. The present complaint with onset, duration and amount of blood loss were also noted. Enquiries were made about menstrual interval, duration of bleeding, passage of clots and number of pads required daily. The medical history included history of recent weight gain or loss, any voice changes, tuberculosis, endocrine disease like diabetes, thyroid disorder, history of any drug intake and any cardiac, renal or haematological disorders. History of any blood or component transfusion and surgical intervention were also recorded, Personal history included history of sexual behaviour, trauma or abortions. Family history was taken in detail regarding presence of any disease like tuberculosis, thyroid disease and bleeding diathesis.

Physical examination included measurement of height, weight and Body mass index (BMI). Pallor, icterus and signs of malnutrition or vitamin deficiency were noted. Neck vein, neck glands, gum bleeding along with pulse, blood pressure and temperature were also recorded. Abdominal palpation was done to exclude any hepatosplenomegaly, ascites or any other abdominal-pelvic mass in the lower abdomen. Skin was examined for purpuric spots. Tenderness over the sternum and other bony areas were examined along with presence of any joint swelling. Obese patients were observed for any signs of acne, hirsutism and features of hyperandrogenism. Secondary sex characters, like breast development, axillary and pubic hairs were inspected. Gynaecological examination included inspection of the vulva and if the hymen appeared intact, vaginal examination was avoided. Speculum and per vaginal

examination were done in those patients who were married.

The baseline investigations in all the cases included- A) Urine for pregnancy test, B) hemoglobin (Hb), complete blood count, peripheral blood smear for red and white blood cell (RBC &WBC) morphology, platelet count, coagulation profile, blood grouping and Rh typing, C) transabdominal USG and serial folliculometry for ovulation status.

In selected cases blood sugar, thyroid profile and hormonal assays including Luteinizing Hormone (LH), Follicular stimulating hormone (FSH) and Prolactin were done. Mantoux test and chest X-ray were advised in suspected cases of tuberculosis. In some selected cases menstrual blood for DNA PCR (Polymerase chain reaction) for Mycobacterium tubercular antigen and endometrial study were done after dilatation and curettage. Bone marrow examination, serum ferritin and Hb-electrophoresis were done in patients having suspected hematological problem. Examination under anesthesia (EUA) and laparoscopy for diagnosis of pelvic mass were planned in unmarried patients and in patients with inconclusive sonography report.

Some investigations (VonWillebrand factor activity, Ristocetin cofactor assay, 21 day serum progesterone level) were done selectively to establish diagnosis in suspected cases. The management protocol was decided upon the condition of the patient and the underlying cause of menorrhagia.

In anovulatory bleeding with a hemodynamically stable patient, antifibrinolytic drugs like tranexamic acid were used as first line therapy during the days of menstruation for control of blood loss. Hormones like combined oral pills (COP), progesterone were prescribed in cases not responding to non-hormonal therapy. Anaemia was corrected by oral haematinics or blood transfusion / component therapy. Treatment of tubercular, haematological and thyroid diseases was done after consulting with respective specialists. Importance was given to provide full nutritional, physical and psychological support to the young girls. Regular check-up of these patients were done by maintaining menstrual calendar, clinical examination and monitoring therapeutic response.

RESULTS AND OBSERVATIONS

Table 1: Age groups

Age group (yrs.)	No. of patient and percentage (%)
10-13	44 (22%)
13-16	84 (42%)
16-19	72 (36%)

From table 1 it is evident that 42% of the patients were in the age group between 13 to 16 years.

Table 2: Age of Menarche

Age of the patient	No. of patient and percentage (%)
<10 yr	3 (1.5%)
10-11 yr	9 (4.5%)
11-12 yr	34 (17.5%)
12-13 yr	85 (42.5%)
>13 yr	69 (34.5%)

42.5% of the patients had menarche between 12-13 years and 34.5% started menstruation after 13 years (Table 2).

Table 3: Duration of symptoms

Duration	No of patient (%)
Less than 6 months	42 (21%)
6 months-1 yr.	134 (67%)
More than 1 yr.	24 (12%)

Table 4: Hemoglobin level of the patients

Hb%	No. of patients	Percentage (%)	
≤5gm/dl	16	8.0%	63.5%
>5-7gm/dl	45	22.5%	
>7-10gm/dl	66	33.0%	
>10gm%	73	36.5%	
Total	200	100%	

From table 3 it is observed that 67% of the patients had menorrhagia for 6 months to 1 year and 63.5% of all patients had haemoglobin level 10 gm % or less (Table 4).

Table 5: Etiological factors

Causes	No. of cases	Percentage (%)
Anovulatory DUB	144	72%
PCOD	21	10.5%
Hypothyroidism	17	8.5%
ITP	6	3.0%
Genital TB	5	2.5%
Cervical Polyp	2	1.0%
Fibroid	4	2.0%
Von Willebrand disease	1	0.5%
Total	200	100%

Anovulatory dysfunctional uterine bleeding (DUB) and polycystic ovarian disease (PCOD) were the two main etiological factors for puberty menorrhagia in our study responsible for 72% and 10.5% of the cases respectively. Six patients (3.0%) had idiopathic thrombocytopenic purpura (ITP) and 8.5% of the patients were hypothyroid. Genital tuberculosis was detected in 5 cases (2.5%) and one patient was diagnosed to have - von Willebrand disease. (Table 5)**.**

Combination medical therapy and surgical therapy: Management of the patients with puberty menorrhagia is depicted in Table 6. 38% (76) of these patients responded well to iron and 3-5 days course of tranexamic acid in the dose of 1.5-2gm daily. 82 (41.0%) patients responded with oral progesterone (norethisterone acetate) for 6-12 cycles and 24 patients (12%) reported good response with combined oral pill (COP). In emergency, conjugated equine estrogen 25 mg intravenously every 6 hourly was administered till the bleeding stopped. Once the bleeding was stopped, norethisterone acetate or combined oral pill was started. All 17 hypothyroid patients were treated with L-thyroxin.

There were 6 ITP patients who were treated with prednisolone with excellent response. Out of them two patients received platelet transfusion. Four ITP patients received oral norethisterone acetate from day 5 to day 25 of the cycle for three cycles. Iron supplementation was given in all patients.

Dilatation and curettage was done in 15 (7.5%) patients for tuberculosis and intractable menorrhagia. Specific surgical procedure like polypectomy and myomectomy was required in 6 (3.0%) patients. Blood component transfusion was given in 72 (36%) patients in the form of packed red blood cell, platelet, fresh frozen plasma or cryoprecipitate.

Table 6: Management of puberty menorrhagia

Type of management	Number of patients	Percentage (%)
Iron+ Folic acid	18	9.0%
Iron+Folic acid+Trenaxamic acid	76	38%
Iron+ Folic acid + Tranexamic acid+ Progesterone	82	41.0%
Iron+ Folic acid+ Tranexamic acid + Combined oral pill (COP)	24	12.0%
Specific (Anti TB-5,Thyroxine-17,ITP-6,Von-Willebrand disease-1)	29	14.5%
Surgery (Polypectomy,Myomectomy)	6	3.0%
Dilatation and Curettage	15	7.5%
Blood Transfusion and Blood Components	72	36.0%

DISCUSSION

Average age of menarche in India is 12.5 years which is comparable to our study. [7] Most of the patient in our study was 13 yrs or above and 29.5% of the patients had Hb% less than 7 gm/dl requiring whole blood or packed red blood cell transfusion. These observations are similar to the observations made by Rao et al and Roychoudhury et al respectively. [2,8] 67% of the patients in our study had symptoms for 6 months to 1 yr and 12% had symptoms for more than 1 year.

72% of the cases of puberty menorrhagia are due to anovulatory DUB in the present study. This is similar to the observations made by Gillani S et al (74.28%). [1] Other studies by Roychowdhury et al and Choudhury et al reported 61.5% and 71% of cases of puberty menorrhagia are due to anovulation caused by immature hypothalamic pituitary ovarian axis. [8,9] All the studies mentioned above are done in this subcontinent and has similar observation whereas Neinstein et al

reported 95% cases of puberty menorrhagia are due to anovulation in North America. [10]

In our study PCOD comprises the second commonest cause of puberty menorrhagia which is similar to Gillani S et al (8.6%). [1] Other studies have regarded bleeding diathesis as second common cause of puberty menorrhagia. [2,8]

Before puberty, LH is secreted primarily at night in an episodic fashion. With the onset of puberty LH peaks increase in a pattern similar to that seen at night due to increase in the frequency and amplitude of pulsatile GnRH (gonadotrophin regulating hormone). The timing of these LH pulses is important in establishing normal ovulatory cycles. Increases in basal LH as well as immature timing of pulses result in anovulatory cycles. [11,12] These cycles are characterized by levels of LH and FSH secretion that are sufficient to induce follicular development and estrogen production but inadequate to induce follicular maturation and ovulation. Thus unopposed estrogen and lack of progesterone in the later phase of menstrual cycle stimulates endometrial growth which ultimately outgrows its blood supply and architectural support, resulting in partial breakdown and shedding in an irregular manner.

In the proliferative phase the endometrium synthesizes equal amounts of PGF2α (Vasoconstrictor and weak platelet aggregator) and PGE_2 (Vasodilator with weak platelet antiaggregatory effect). However in the luteal phase the levels of PGF2α progressively increase under the influence of estradiol and progesterone. In anovulatory DUB the lack of progesterone results in decrease in the PGF2α resulting in increased mean menstrual blood loss. [3] It is also responsible for the absence of uterine contractions and painless period characteristics of anovulatory menstruation.

In PCOD, ovaries typically have multiple follicular cysts less than 10 mm in size and increased stroma. It is associated with chronic anovulation which may result from an increased pulsatility of GnRH. This results in elevated LH levels and increased ovarian androgen production. [11] The primary menstrual irregularity in these patients is oligomenorrhoea, although about 5% may demonstrate polymenorrhoea. This may be temporary in adolescents or may eventually progress to advanced polycystic ovarian disease. Diagnosis is confirmed with altered luteinizing hormone (LH) and follicle stimulating hormone (FSH) ratio on day 2 of the cycle. [3]

The primary management of anovulatory bleeding is to control symptoms and prevent anemia. In adolescents with mild bleeding, reassurance and prophylactic iron treatment are suitable. However in patients who are sexually active or symptomatic for 3 to 6 months with anemia (Hb 7-10 gm/dl) require cyclical norethisterone acetate or COP in addition to iron and folic acid.

Antifibrinolytic like tranexamic acid are a newer form of treatment in puberty menorrhagia. Plasminogen activators are a group of enzymes that cause fibrinolysis. An increase in the levels of plasminogen activators has been found in the endometrium of patients with heavy menstrual bleeding compared to those with normal menstrual loss. Plasminogen activators have been therefore been prompted as a treatment in heavy menstrual bleeding. [13]

Hormones either in the form of progesterone or COP constitute the main medical therapy in the treatment of puberty menorrhagia along with hematinics and tranexamic acid. Various studies suggest that these are of value in arresting profuse hemorrhage. [14] Hormonal therapy restores the balance between prostaglandins and thromboxane

A2 and stabilizes the menstrual cycle. COP was administered to 12% patients in the present study whereas 41% of the patients had received norethisterone acetate.

The best treatment modality in puberty menorrhagia due to PCOD is COP because it inhibits LH and decreases circulating testosterone level. Sex hormone -binding globulin is also increased and available to bind and inactivate testosterone in the circulation. [15] COP does not aggravate the underlying insulin resistance significantly and may attenuate some of the lipid derangements induced by sustained excess androgen exposure. [16]

Progesterone can be used cyclically in two different treatment protocols: as a short course during the luteal phase and a relatively longer course lasting 21 days from day 5 of the cycle. In patient with severe bleeding associated with hemodynamic changes, blood transfusions are indicated with administration of intravenous conjugated estrogens in a dose of 25 mg every 6 hours until bleeding stops for 24 hours. [17] Once bleeding is controlled, the patient is started on a regimen of strong androgenic progestogen or COP.

Another treatment option to control abnormal bleeding is cyclic medroxyprogesterone acetate 10 mg orally for 10 days from day 15 of each month. There are some reports expressing doubts about the efficacy of medroxyprogesterone, so we have used norethisterone though it has more androgenic effect than medroxyprogesterone. [18] Medroxyprogesterone also does not alleviate the associated androgenic effects of polycystic ovaries. [19]

In the present study, we have used oral norethisterone acetate 10 mg three times daily for 14 days for control of heavy bleeding followed by oral norethisterone acetate 5 mg thrice daily or COP for 6-12 cycles. We have preferred norethisterone for anovulatory DUB and COP for PCOD. We have avoided danazole because of its masculinizing side effects in adolescent girls.

Majority of patients in the present study received a combination therapy of tranexamic acid and norethisterone acetate or COP. Our observations are also similar to previous studies. [1,2,8] Incidence of hypothyroidism and tuberculosis are similar in our study and Roychoudhury et al. [8] But the incidence of hypothyroidism is much less (2.86%) in the study made by Gillani S et al compared to present study. [1] This difference is probably due to difference in the prevalence of hypothyroidism in Peshawar and south Bengal.

The menorrhagia associated with hypothyroidism responds promptly to the thyroid replacements, often in doses insufficient to correct the other manifestations of this condition. This suggests that thyroxin does have a direct effect on the spiral arterioles and on hemostasis in menstruation. [14]

In our study there were five cases of genital TB which were treated with Anti-Koch's therapy along with COP. The incidence of genital TB is about 1% amongst the gynecological patients attending the outpatient department in developing countries. [20] Menorrhagia or irregular bleeding in genital TB is probably due to ovarian involvement, pelvic congestion or endometrial lesions.

The occurrence of excessively heavy irregular periods should prompt an evaluation of hematological status to rule out blood dyscrasias. In our study there were 6 patients diagnosed to have ITP. 80% patients of ITP have menorrhagia. [14] Acute ITP is most commonly seen in young and caused by immuno complexes containing viral antigens that bind to the platelet Fc receptors, or by antibodies produced against viral antigens that cross react with platelets. It can be associated with infectious mononucleosis, acute

toxoplasmosis, CMV infections, viral hepatitis and HIV. [21]

Incidence of blood dyscrasias in our study is comparatively less than the previous studies in this subcontinent. [1,2,8] But there is gross reported variation in the incidence of blood dyscrasia in the previous studies also. Claessens and Cowell reported 19% of adolescents with menorrhagia requiring hospitalization had an underlying coagulation disorder in their study whereas a more recent retrospective study by Falcone et al found that 4.9% of admissions due to puberty menorrhagia over a 10 year period were secondary to a coagulopathy. [19,22]

VonWillibrand disease was detected in one patient in our study. Similar incidence of this rare hematological disorder was reported in previous study. [1]

All the previous studies on puberty menorrhagia reported in this subcontinent have a small sample size compared to present study. Roychoudury et al has highest sample size of 68 patients reported till date to the horizon of our knowledge compared to 200 patients in our study.

CONCLUCION

We can conclude from the present study that commonest cause of puberty menorrhagia is immaturity of the hypothalamic - pituitary ovarian axis resulting in anovulation. Underlying endocrine, hematological, pregnancy associated disorder and tuberculosis are other causes to be searched for when assessing a case of puberty menorrhagia. Anatomical abnormalities like fibroid or polyp are also to be ruled out. Once the diagnosis is made medical or surgical treatment as appropriate is to be administered.

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