

# Evaluation of Hypothalmo-Pituitary Gonadal Axis Immaturity as an Aetiological Factor in Menstrual Irregularities in Early Adolescent Girls

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## ABSTRACT

**Introduction:** Menstrual irregularities during early pubescence remains a common presentation associated with pubertal transitional phase of reproductive endocrine system in terms of changes in HPG axis posing a challenge to make a diagnosis during the 1-2 years following menarche in clinical setup. Study aimed to explore the interplay of neurological and hormonal causes which is crucial in reaching a proper diagnosis amongst other causes of puberty menorrhagia and to evaluate its medical management.

**Material and Methods:** A retrospective analysis was carried out for etiological factors and duration of menorrhagia, age of menarche along with investigation profile and modalities of management from the medical records of 40 patients who presented with menorrhagic cycles in the pubertal age group.

**Results:** In 29 patients etiology was found to be anovulation secondary to immaturity of hypothalamic pituitary gonadal axis while 4 had hypothyroidism, 3 had PCOS. Out of 3 patients of coagulation defects 2 had thrombocytopenia, one Von willebrand disease and 1 patient had symptomatic fibroid polyp.

**Conclusion:** Puberty menorrhagia is a distressing condition which can lead to severe complications. The menstrual irregularities in adolescents are mainly influenced by the complex interplay of a number of factors governing maturation of the hypothalamic pituitary ovarian axis which involves changes in the excitatory and inhibitory neurotransmitters that regulate GnRH release.

**Keywords:** Hypothalmo-Pituitary, Gonadal Axis Immaturity, Aetiological Factor, Menstrual Irregularities

## INTRODUCTION

During pubertal stage the reproductive endocrine system shows transition from a, comparatively dormant, non-cyclic state to a state of cyclic reproductive function. This is marked by the onset of pulsatile gonadotropin secretion due to increase in GnRH pulse frequency and pulse amplitude from hypothalamus, leading to maturation of HPG axis hence sexual maturation.

During this pubertal transition, it is common for adolescents to present with menstrual irregularities.<sup>1</sup> It is crucial for the clinicians to have thorough knowledge of the various etiological factors of pubertal menstrual problems in reaching a proper diagnosis during this period. The common causes include anovulatory cycles, bleeding disorders, polycystic ovarian syndrome, endometrial and hypothyroidism.<sup>2,3</sup>

Bleeding is usually heavy, causing anaemia and may require blood transfusion. Among the inherited bleeding disorders platelet defects are the most common causes of puberty menorrhagia.<sup>4</sup> This study aimed at exploring the magnitude of role played by immature HPG axis amongst the other causes of responsible for menstrual irregularities in the adolescent girls in our set-up and also the role of conservative management in

them.

## MATERIAL AND METHODS

Three year retrospective analysis was carried out from the medical records of 40 young girls from the age of menarche to 19 years of age with history of excessive bleeding per vaginum attending the outpatient (OP) ward or admitted in the Dept of Obstetrics and Gynaecology of MMMC and Hospital, Kumarhatti. A detailed analysis regarding demographic profile, age, socioeconomic status, age of menarche, previous menstrual history, menstrual interval, duration of bleeding passage of clots number of pads required daily was done. Physical examination included calculation of BMI of the individual. Inclusion criteria were - History of flow of more than seven days duration, History of passage of clots and Hb of 10 gm% or less. Routine as well as specific investigations that were done included Hb, PCV, a total and differential count, platelet count, peripheral smear, PT, APTT, blood sugar, S. TSH LH, FSH, S. prolactin and ultrasound abdomen and pelvis. Some investigations done in selected patients included chest X ray, menstrual blood for TB PCR and Mantoux.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used to make tables. Descriptive statistics like mean and percentages were used to interpret the data.

## RESULTS

A total of 40 patients with pubertal menorrhagia were analyzed. The age of onset of menarche of less than 10 years of age was seen in 15%. 50% patients had menarche after the age of 12 years (Table 1). Duration of menarche was less than one year in 57.5% of the cases (Table 2). In 29 patients the cause was thought to be immaturity of the HPO axis as they had a normal study on ultra-sound and their hormonal assays were within normal limits while 3 were diagnosed due to PCOS based on

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**How to cite this article:** Anjana Mittal, Gurdev L. Goyal, Lajya Goyal, Shamim Monga. Evaluation of hypothalmo-pituitary gonadal axis immaturity as an aetiological factor in menstrual irregularities in early adolescent girls. International Journal of Contemporary Medical Research 2016;3(11):3236-3238.

ultrasound criteria. 4 Patients had elevated TSH levels with normal T4 and T3 values. 1 patients had Polyp uterus (Table 3). Twenty five patients presented with the history of menorrhagia since less than 6 months while fourteen presented at first episode (Table 4).

## DISCUSSION

Abnormal menstrual bleeding in adolescents can be caused by a number of conditions. Most of the cases are due to anovulatory cycles with immaturity of the hypothalamo-pituitary-ovarian-endometrial axis.<sup>5</sup> Anovulatory bleeding was responsible for 50-74 % of patients requiring hospital admission as reported in the literature.<sup>2,3</sup> In our study the incidence of menorrhagia due to anovulation secondary to immaturity of hypothalamic pituitary ovarian endometrial axis has been comparable (72.5%) to some other studies reporting the incidence as 61.5% and 71%.<sup>6,7</sup> The immaturity of HPG axis leading to immature timing of LH pulse as well as increase in basal plasma LH levels results in anovulatory and irregular menstrual cycles. Although all three HPG levels become active during the pubertal period, the driving force is the hypothalamic GnRH neurons.<sup>8,9</sup> However, GnRH neurons have the ability to release the GnRH decapeptide long before puberty. Therefore, the attainment of reproductive competence involves not only molecular modifications of gene and protein expression of GnRH, but also, a maturation of the hypothalamic neural circuitry that regulates the GnRH cells.<sup>10,11</sup> Puberty involves changes in the excitatory and inhibitory neurotransmitters that regulate GnRH release, is characterized by decreased GABAergic inhibition of GnRH neurons, and an enhancement of facilitatory effects of glutamatergic inputs to

the GnRH system, among other neurotransmitters that modulate the timing of puberty.<sup>12</sup> As the reproductive system matures, a pulsatile pattern of gonadotropin secretion is established, the LH surges gradually come at regular intervals, and cyclic reproductive function becomes firmly established which continues throughout reproductive life into menopause.

Menorrhagia associated with hypothyroidism may either be due to breakthrough bleeding or due to decreased levels of certain clotting factors.<sup>13</sup> In our study incidence of hypothyroidism was 10% patients which was comparable to that (7.15%) of another study conducted on 70 cases of pubertal menorrhagia.<sup>14</sup> Menorrhagia associated with hypothyroidism respond promptly to thyroid hormone therapy, indicating direct effect of thyroid on arterial system as well as hemostasis at menstruation.

The incidence of bleeding disorder in adolescent menorrhagia varied from 17-25% in the various studies of past and recent literature.<sup>15,16</sup> In present study three patients presented with bleeding disorders with two of them having thrombocytopenia while Bevan et al found 13% incidence of thrombocytopenia among all girls who presented with menorrhagia.<sup>17</sup>

Polycystic ovarian disease as a cause of menorrhagia might have been developed from temporarily condition of polycystic ovaries in early adolescent. In our study menorrhagia due to PCOS was higher (7.5%) compared to that found in the studies done by Rao and Chowdhury as 2.8%, and 3.07% respectively.<sup>6,7</sup> Diagnosis was confirmed by hormonal assay and ultrasonography. Progestogens are generally effective but can be used in combination with estrogen as combined OCP's. COCP's were chosen as first line therapy along with haematinics. Although rare, uterine pathology such as fibroids and polyps may lead to abnormal uterine bleeding.<sup>18</sup> Our patient with symptomatic polyp uterus responded to underwent polypectomy. Mainstay of treatment in puberty menstrual irregularities remains hormonal therapy directed towards stabilizing the endometrium and treating the hormonal alterations.

## CONCLUSION

The fact that most of the cases of menstrual irregularities in adolescents are due to anovulatory cycles with immaturity of the hypothalamo-pituitary-ovarian-endometrial axis being modulated by the various neurotransmitters of central nervous system remains crucial in making diagnosis in our clinical set up while ruling out the other causes like hypothyroidism, bleeding disorders and other reo-endocrine dysfunctions.

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Age at men-arche	Number of patients	Percentage
<10 years	6	15%
10-12years	14	35%
12-14 years	20	50%

Table-1: Age at menarche

Duration of menarche	No of Patients	Percentage
Less than 6 months	5	12.5
6 months- 1 year	18	45
1-2 Years	11	27.5
More than 2 years	6	15

Table-2: Duration of Menarche

Etiological factor	Number of patients	Percentage
Ovulatory dysfunction including PCOS	32	80
Hypothyridism	4	10
Coagulation abnormalities	3	7.5
Endometrial	1	2.5
Not classified	0	0
Iatrogenic	0	0

Table-3: Etiological factors

First episode	14
3-6 months	11
6-12 months	9
>12 months	6

Table-4: Duration of Menorrhagia

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**Source of Support:** Nil; **Conflict of Interest:** None

**Submitted:** 11-09-2016; **Published online:** 25-11-2016