Abnormal Uterine Bleeding Among Adolescents in Kashmir: A Tertiary-Care Hospital Based Study

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is one of the most common disorders in adolescent population and forms the bulk of gynecological abnormalities in this age group. However, the epidemiological data on AUB in adolescents is scarce especially in the Indian subcontinent. This single-center prospective observational study was conducted to evaluate the contribution of various etiological factors in AUB in this part of the world using the PALM-COEIN classification where PALM represents structural causes: polyp, adenomyosis, leomyoma and malignancy and COEIN represents functional causes: coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and "not yet classified" entities. **Methods:** Females in the age group of 10 to 19 years who presented with AUB were enrolled from January 2016 to December 2016. The etiology of AUB was sought through a detailed history, clinical examination and laboratory evaluation which included routine tests, hormonal analysis and ultrasonography of the abdomen and pelvis in all cases. CT and MRI was done whenever deemed necessary. **Results:** A total of 195 patients were enrolled (mean age =14.3 ± 4.6 years). Functional causes accounted for the majority (98.47%) of the causes of AUB in adolescent girls: Polyp = 1 (0.51%), Adenomyosis = 0, Leomyoma = 1 (0.51%), Malignancy = 1 (0.51%), PALM = 3 (1.53%) and Coagulopathy = 3 (1.54%), Ovulatory disorder = 178 (91.28%), Endometrial = 0, Iatrogenic = 3 (1.53%), Non-specified = 8 (4.10%), COEIN = 192 (98.47%). Ovulatory disorders which formed the bulk of the patients were mostly due to immaturity of hypothalamic-pituitary-ovarian axis (54.49%) followed by polycystic ovarian syndrome (33.14%) and thyroid disorders (12.35%). On USG, bulky ovaries, with polycystic morphology (35.38%), isolated ovarian cysts 20 (10.25%) and fibroids 1(0.51%) were the abnormalities found. **Conclusion:** Ovulatory disorders are the most common cause of AUB in adolescent population. Structural causes, although very infrequent, need to be ruled out. PALM-COEIN classification is a useful tool for systematic approach to evaluate patients with AUB.

Keywords: Abnormal uterine bleeding, Adolescence, Polycystic ovarian syndrome, PALM-COEIN, leiomyoma.

INTRODUCTION

Adolescence is the time of life between puberty and psychophysical maturity, when crucial somatic, metabolic, endocrinological and psychological changes occur in females. Healthy reproductive function is the expected end point of this process.[1-3] Menstrual disorders are among the most frequent gynecological complaints in this age group.[1-3] Adolescents may have amenorrhea, dysmenorrhoea, or abnormal uterine bleeding (AUB) which is defined as bleeding from the uterine corpus that is abnormal in duration, volume, frequency and/or regularity.[1-3] AUB accounts for half of the gynaecologic problems among adolescents.[1-7] It may be caused by a variety of gynecological and non-gynecological causes, systemic diseases, endocrine disorders and medications.[1-7]

In order to create a universally accepted nomenclature and to standardize evaluation and management of AUB, International Federation of Gynecology and Obstetrics (FIGO) and American college of Obstetrics and Gynecology (ACOG), introduced the "PALM-COEIN" classification.[2] Here PALM represents structural causes: polyp, adenomyosis, leomyoma and malignancy whereas COEIN represents non-structural causes: coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and "not yet classified" entities.[2] The PALM-COEIN classification has been found to be useful when evaluated and validated in India especially in adult and peri-menopausal age-group.[8] However, there is still paucity of epidemiological data on AUB in adolescents from the Indian subcontinent. This hospital based prospective observational study was conducted keeping in view those lacunae in the literature. The study was designed to look into the contribution of structural (PALM) and functional (COEIN) components of etiology of AUB in adolescent females at a single tertiary-care hospital in North India.

MATERIALS & METHODS

We aimed to evaluate adolescent females who presented to our centre for AUB and classify their

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etiology according to PALM COEIN nomenclature. It was a prospective observational study involving a single centre (Lalla Ded Hospital, Government Medical College, Srinagar), a tertiary-care hospital and one of the few referral centers for Obstetrics and Gynecology in Jammu and Kashmir. The study had the approval of the Institutional Ethical Committee.

Subjects

Adolescent females, 10 to 19 years of age, who presented with clinical features suggestive of AUB to either out-patient or in-patient facilities at our centre were enrolled. Written informed consent was taken from every patient or the caregiver, whichever was applicable, at the time of enrollment. Patients already on hormonal therapy, those who had delivered or aborted within last 6 weeks and those with primary amenorrhea were excluded from study. A detailed history, systemic examination and routine laboratory tests including haemogram, blood counts, kidney and liver function tests, fasting blood sugar was done in all patients. All patients underwent a battery of investigations which included FSH, LH, prolactin, testosterone levels, thyroid profile, coagulation profile, fasting insulin level and cortisol level. Ultrasound of abdomen and pelvis was done in all cases. Computed tomography (CT) or magnetic resonance imaging (MRI) was advised whenever necessary.

The recorded data was analyzed using the SPSS software (version 22.0, IBM Corporation, New York, United States). Continuous variables were expressed as mean ± standard deviation and categorical variables were summarized as frequencies and percentages.

RESULTS

A total of 356 subjects in the study age-group attended to our centre with menstrual abnormalities from January 2016 to December 2016 (flowchart). Out of these 276 consented for inclusion into the study. On further history and clinical examination only 195 could be classified as AUB (flowchart).

Table 1: Demographic, clinical features and hormonal profile of patients (N = 195). Mean age = 14.3 ±4.6 years

			Number (Percentage)
Age group		10-12 years	23 (11.79)
		13-15 years	97 (49.74)
		16-19 years	75 (38.46)
Age at menarche		10-12 years	58 (29.74)
		13-15 years	133 (68.20)
		16-19 years	4 (2.05)
Duration of menstrual flow		<3 days	71 (36.41)
		3 -5 days	86 (44.10)
		>5 days	38 (19.79)
Length of cycle		< 21 days	38 (19.48)
		21-35 days	80 (41.02)
		>35days	77 (39.48)
History		Bleeding diathesis	2 (1.02)
		Weight gain, acne, hirsutism	67 (34.35)
		Emergency contraceptive pill intake	3 (1.53)
Hormonal profile	LH/FSH ratio	Normal	133 (68.20)
		Raised	55 (28.20)
		Decreased	7 (3.58)
	TSH	Normal	173 (88.71)
		Raised	21 (10.77)
		Decreased	1 (0.51)
	Serum testosterone	Normal	175 (89.74%)
		Raised	19 (9.74)
		Decreased	1 (0.51)
	Prolactin	Normal	186 (95.38)
		Raised	7 (3.59)
		Decreased	2 (1.03)

Table 2: USG findings of adolescent patients with abnormal uterine bleeding (N = 195)

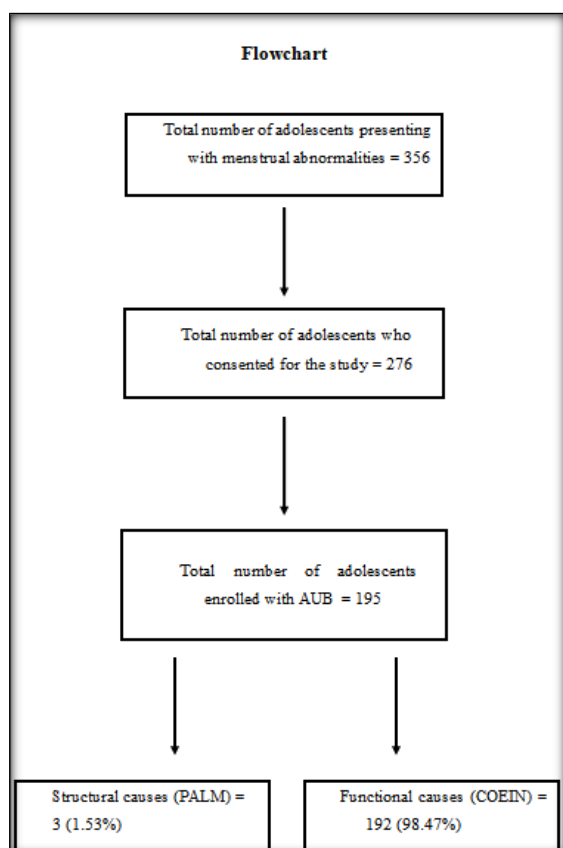| USG findings	Frequency (Percentage)
Bulky ovaries with polycystic ovarian morphology	69 (35.38%)
Leiomyoma	1 (0.51%)
Isolated single ovarian cyst	20 (10.25%)
Polyp	01 (0.51%)
Normal USG	104 (53.33%)
Total	195

The mean age of cases was 14.3 ± 4.6 years. Most of the patients in our study were of 13 to 15 year age-group (49.74 %) followed by 16 to 19 year age-group (38.46%). Most of the girls (68.20 %) had attained their menarche between 13 to 15 years of age. Bleeding lasted for 3-5 days in most (44.10 %) of the patients with majority of the subjects having cycle length of 21 to 35 days (41.02 %) [Table 1]. History of intake of drugs like emergency contraceptive use was seen in 3 patients (1.54%) [Table 1]. Features of hyper-androgenism like acne, hursuitism, weight gain were present in 67 patients (34.35%), most of whom also demonstrated PCOS morphology on ultrasound [Table 2]. In the

hormonal profile of patients, majority (68.20%) had normal LH/FSH ratio and in about 28.20% patients had raised LH/FSH ratio. Serum prolactin and testosterone was also found to be normal in majority of patients. Only 19 patients (9.74%) and 7 (3.59%) had raised testosterone and prolactin levels respectively (Table 1). History of bleeding diathesis like epistaxis, easy bruisability and gum bleeding was present in only 2 patients (1.02 %) [Table 1].

Table 3: Frequency of the causes of abnormal uterine bleeding when classified as per the PALM-COEIN classification (N = 195).

PALM-COEIN classification		Frequency (Percentage)	
PALM	Polyp	1 (0.51%)	3 (1.53%)
	Adenomyosis	0 (0%)	
	Leomyoma	1 (0.51%)	
	Malignancy	1 (0.51%)	
COEIN	Coagulopathy	3 (1.53%)	192 (98.47%)
	Ovulatory Disorder	178 (91.28%)	
	Endometrial	0 (0.0%)	
	Iatrogenic	3 (1.53%)	
	Non-specified	8 (4.10%)	
Total		195	

Flowchart

Total number of adolescents presenting with menstrual abnormalities = 356

Total number of adolescents who consented for the study = 276

Total number of adolescents enrolled with AUB = 195

Structural causes (PALM) = 3 (1.53%)

Functional causes (COEIN) = 192 (98.47%)

USG of pelvis did not show any abnormality in majority of patients (53.33%). Bulky ovaries, with polycystic morphology, were seen in almost 1/3rd of the patients (35.38%). Isolated ovarian cysts and fibroids were found in 20 patients (10.25%) and 1 patient (0.51%) patients respectively [Table 2]. Ovulatory disorder was the main cause of AUB among adolescent girls accounting for 88.72% of

cases [Table 3]. This was mostly due to immaturity of hypothalamic pituitary ovarian axis (54.49%) followed by PCOS (33.14%) and thyroid disorders (12.35%) [Table 4]. On classification of the etiology of AUB according to the PALM-COEIN nomenclature, PALM (structural causes) accounted for 1.53% and COEIN (functional causes) accounted 98.47% causes of AUB in adolescent girls [Table 3].

Table 4: Ovulatory disorders in adolescent patients with abnormal uterine bleeding (N = 178/195) (HPO: Hypothalamic pituitary ovarian, PCOS: Polycystic ovarian syndrome)

Ovulatory Disorders	Frequency (Percentage)
Immaturity of HPO axis	97 (54.49%)
PCOS	59 (33.14%)
Thyroid disorders	22 (12.35%)
Total	178

DISCUSSION

AUB is a common disorder in adolescents with significant morbidity leading to complications like anemia.[3-7] It is one of the common causes of hospitalization in adolescent females.[3-7] We searched PUBMED using the terms "abnormal uterine bleeding", "adolescent", "India" and "PALM COEIN". We did not find any prospective study conducted in the Indian subcontinent for evaluation of etiology of AUB done exclusively in adolescent subjects. Prospective studies in other parts of the world investigating etiology of adolescent AUB when stratified as per the PALM-COEIN classification are also scarce. However our results are similar to other studies conducted across the world prior to the PALM-COEIN classification with non-structural cases being much more common than the structural causes.[3-7] These cases form more than 95 % of our patients. Ovulatory disorders especially immaturity of hypothalamic-pituitary-ovarian axis form the bulk of these non-structural causes. Anovulatory cycles which are either physiological or due to pathologies like PCOD result in a hormonal tilt in favor of oestrogens like estradiol which cause endometrial epithelial cell proliferation, gland growth and vascularisation as compared to progesterone which stabilizes the thickened endometrium and expedites clot formation and stabilization. This results in an unchecked proliferation of the endometrium and unpredictable bleeding in the early reproductive years.[3] PCOS forms almost half of our patients with ovulation disorders. This high prevalence should not be surprising given high prevalence of PCOS, probably higher than elsewhere in the world, in Kashmiri women, as had already been documented.[9] This high prevalence in reproductive age group may be related to both genetic and environmental factors specific to the region.[9] Thyroid dysfunction is one of the most common causes of menstrual abnormalities in all age groups of women.[10,11] Both

hyper and hypothyroidism can result in menstrual abnormalities with hypothyroidism being more commonly associated with AUB. AUB can be the presenting manifestation of thyroid dysfunction preceding all other symptoms.[10,11] It is therefore obligatory to evaluate all patients with AUB for thyroid disorders. Prompt treatment of thyroid dysfunction usually resolves menstrual abnormalities. Menstrual abnormalities in adolescents may also be the presenting manifestation of a serious underlying coagulation disorders like von Willbrand disease.[12-14] It is pertinent to evaluate all adolescent females for these disorders if they present with AUB. Three patients in our study group had deranged coagulation parameters like bleeding time, clotting time and international normalized ratio (INR) with normal imaging and hormonal profile. All the three cases were referred for expert evaluation by a hematologist.

Although only a handful of cases are reported in literature,[15-16] we found 1 cases of symptomatic leiomyoma in our cohort of patients. We did not see any patient with adenomyosis which is a very infrequent cause of AUB in adolescents. It is essential to rule out these structural causes by prompt imaging in all adolescents with AUB and follow up with sampling for Histopathological diagnosis. Complications necessitating surgical interventions have been reported in adolescents with leiomyoma.[15,16]

CONCLUSION

Menstrual problems among adolescent girls are very common and a significant source of morbidity. AUB is more common in the initial 2 years post-menarche. Non-structural causes like anovulatory bleeding due to immaturity of HPO axis, PCOS and thyroid dysfunction are the most common causes in adolescent girls. It is essential to rule out structural causes like leiomyomas although they are infrequently the source of bleeding. A thorough clinical evaluation supplemented by imaging and laboratory tests like hormonal levels, thyroid function tests and coagulation parameters, is essential to reach a timely diagnosis.

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