ORIGINAL ARTICLE

Study on Pattern of Primary Amenorrhea at Tertiary Care Center—A Retrospective Analysis

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ABSTRACT

Introduction: Primary amenorrhea is defined as lack of attainment of menarche by the age of 15 years in a patient with appropriate development of secondary sexual characteristics and 13 years in the absence of secondary sexual characters. The present study is undertaken to study the etiological features, associated anomalies and treatment options for patients with primary amenorrhea.

Objectives

- To determine the incidence of etiological factors of primary amenorrhea.
- To determine the association of various anomalies with primary amenorrhea.

Methodology: It is a retrospective study planned to be conducted from Jan 2011 December 2015, in the Department of Obstetrics and Gynaecology, Vydehi Institute of Medical Sciences and Research Centre.

Results: In our study group I, i.e., eugonadotrophic group consists of 34 patients (77.2%), group II, i.e., hypergonadotrophic group has 9 (20.45%) patients and 1 patient in hypergonadotrophic group, i.e. group I.

In group I mean FSH, LH estradiol , prolactin and TSH values are 6.89 miu/mL, 8.8 miu/mL, 45 pg/mL, 20.8 ng/mL, and 3.05 iu/mL. In group II mean values of FSH, LH, estradiol, prolactin, and TSH are 51.82 miu/mL, 13.3 miu/mL, 12.7 pg/mL, 22.1 ng/mL and 5.4 iu/mL.

Conclusion: Primary amenorrhea is an extremely stressful situation for young girls and needs psychological counseling to prevent long term sequelae. The feeling of defeminization and underdevelopment of secondary sexual characters is the major concern in patient and attendees is the major concerns which has to be addressed with careful counseling.

Keywords: Adolescent gynecology, Gonadotropins, Gynecological endocrinology.

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INTRODUCTION

Adolescence is the milestone of women hood, which starts with the attainment of reproductive maturity called puberty. Menarche is the most important event in puberty. Primary amenorrhea is defined as lack of attainment of menarche by the age of 15 years in a patient with appropriate development of secondary sexual characters and 13 years in the absence of secondary sexual characters. The prevalence of primary amenorrhea is 1–3%.[1] It is not a disease but a clinical symptom that may result from various causes. Normal menstruation depends on the structural and functional integrity of the female genital tract, ovaries, pituitary gland, and hypothalamus. Disturbances in any of the above components or abnormalities in the chromosomal constitution may result in primary amenorrhea.[1,2]

Worldwide gonadal dysgenesis is the most common cause of primary amenorrhea, and Mullerian developmental disorders, and androgen insensitivity syndrome are second and third the common, respectively.[3] Apart from this incidence of the disease may also depend on racial, genetic and environmental factors. The incidence of Mayer–Rokitansky–Kustner–Hauser syndrome (MRKH) varies from 1 in 4000 to 1 in 5000 female births. In type 1 MRKH or the typical form (also known as Rockitansky sequence); only the caudal part of the Mullerian duct (upper vagina and uterus) is affected. Type 2 or atypical form is associated with vertebral, cardiac, neurological abnormalities. The incidence of anatomical abnormalities varies depending on the type of anomaly. The incidence of Imperforate hymen is between 0.3% and 0.8% and that of the transverse vaginal septum is 2 in 1,00,000 female births. Chromosomal factors are the etiological problem in 16–50% of women presenting with primary amenorrhea.[3,4]

Primary amenorrhea is a rare problem, which needs to be addressed regarding menstrual problems and future reproductive outcomes. Although it is a well-recognized

problem, there are not many studies on it. The present study was undertaken to determine the etiological factors responsible for primary amenorrhea and its association with other anomalies. It is taken as an opportunity to counsel the girl and her parents to prevent long-term psychological sequel.

OBJECTIVES

- To determine the etiological factors of primary amenorrhea.
- To determine the association of various anomalies with primary amenorrhea.
- To counsel the girl and parents regarding future menstrual, coital and reproductive outcomes.

METHODOLOGY

It is a retrospective study conducted in the Department of Obstetrics and Gynaecology, Vydehi Institute of Medical Sciences and Research Centre from January 2011–December 2015. As it is the routine policy in our institution to admit the patient for evaluation of primary amenorrhea because our patients are from distant areas and they were willing for admission for evaluation. Case sheets were retrieved retrospectively, and the data was collected. Preliminary details were entered like the age of presentation, occupation. Address, socioeconomic status, presenting complaints, family history, and other significant past history were documented in detail. On general physical examination weight, height, body mass index (BMI), features of Turner's syndrome, the presence of hirsutism were documented. Development of breast was documented according to Tanner stages I–V. External genitalia examined (normal/infantile). Development of pubic hair was documented (Tanner stages I–IV).

The internal examination was done only in married patients and ultrasound, i.e., transabdominal ultrasonography was done in all the patients and following features were documented–uterus (normal/hypoplastic), vagina (normal, hypoplastic, blind, absent), ovary (normal, streak, absent). Obstructive features like hematometra/hematocolpos were documented. Associated pelvic findings and other abnormalities were documented. Laboratory tests like thyroid profile, serum FSH, serum LH, serum prolactin done for all the patients. Relevant investigations were done based on clinical suspicion and karyotyping was done for all the patients and they were divided

into 3 groups eugonadotropic FSH (5–40 miu/mL) i.e., group I, hypergonadotropic (FSH of > 40 miu/mL), i.e., group II and hypogonadotropic (FSH of <5miu/mL) i.e. group III, the results were statistically analyzed.

Treatment options were given for participants in each group. In group I patients with sufficient vaginal length and rudimentary uterus were counseled about their possibility of coital function and reproductive function (through surrogacy). The patients with short vaginal length were advised serial dilatation of the vagina. Patients with blind vagina were advised vaginoplasty, 3 months before their marriage. Patients presenting with obstructive symptoms were corrected surgically. In group II, patients with XO karyotyping were offered medical management with hormonal therapy and patients with XY karyotyping were advised to undergo gonadectomy, because of malignancy risk in dysgenetic gonads. In group III participants were offered medical management with hormonal therapy.

Statistical Analysis

The data were entered in Microsoft XL file and converted to Statistical Package for the Social Sciences (SPSS). The data were analyzed using SPSS version 21. All categories of variables expressed as frequencies and percentages. Continuous variables were expressed as mean ± standard deviation. As three groups were different with respect to clinical presentation, hormonal profile and treatment options, so the comparison was not done in between the groups. For comparison statistically, a minimum of 8 participants should be present in each group, as group III has only one participant statistical comparison is not possible between each group.

RESULTS

In our study, group I, i.e., eugonadotropic group consists of 34 patients (77.2%), group II, i.e., hypergonadotropic group has 9 (20.45%) patients and 1 patient in Hypogonadotropic group i.e., group III.

Mean age of presentation in group I was 21.58 years, and height was 151.41 cm, mean weight was 51.85 kg and BMI–22.65 kg/m^2. Mean age of presentation in group II was 20.74 years, mean height was 147 cm, mean weight 38.77 kg and BMI was 17.88 kg/m^2. In group III the mean age of presentation was 23, mean height 146 cm, mean weight 41 kg and BMI was 19.2 kg/m^2 (Table 1).

Table 1: Basic Details

Group	Number of participants	Age (years)	Height (cm)	Weight (kg)	BMI (kg/M^2)
I	34 (77.27%)	21.58 +/– 4.8	151.41 +/–6.9	51.85 +/–7.08	22.65 +/–2.74
II	9 (20.45%)	20.77 +/– 3.76	147.33 +/–5.56	38.77 +/–8.80	17.68+/–3.12
III	1 (2.2%)	23	146	41	19.2

Table 2: Clinical presentation in each group

Group	Presenting complaint	B.D (Tanners stage)	AH (P–present) (A–absent)	PH (Tanners stage)
Group I	Primary amenorrhea 34 (100%) Pain abdomen 8 (23.5%) Dysmenorrhea and dyspareunia 4 (11.7%)	I–0 (0%) II–1–2.9 III–3-38.21 IIII–20-58.81%	P–33 (91.05%) A–1 (2.9%)	I–0 (0%) II–1 (2.97%) III–12 (35.3%) IV–21 (61.7%)
Group II	Primary amenorrhea–9 (100%) Absent secondary sexual characters 9 (100%) Hirsutism 3 (33.3%) Distension of abdomen 1 (11%)	I–7 (77.7%) II–2 (22%) III–0 (0%) IV–0 (0%)	P–7 (77.1%) A–2 (22.2%)	I–7(77.%)2 II–0 (0%) III–2 (22.2%) IV–0 (0%)
Group III	Primary amenorrhea–1 (100%) Absent secondary sexual characters–1 (100%)	I–0 (0%) II–1 (100%) III–0 (0%) IV–0 (0%)	P–0 (0%) A–1 (100%)	I–1 (100%) II–0 (0%) III–0 (0%) IV–0 (0%)

Table 3: Hormonal profile of groups

Group	Mean FSH (miu/mL)	Mean LH (miu/mL)	Serum estradiol (pg/mL)	Serum prolactin (ng/mL)	TSH (miu/mL)	Karyotyping
I	6.89 +/– 1.72	8.80 +/– 4.86	45.52 +/– 11.6	20.82 +/– 6.4	3.05 +/– 1.28	46XX–34 (100%)
II	51.82 +/– 24.0	13.31 +/– 7.95	12.77 +/– 13.41	22.13 +/– 6.32	5.4 +/– 3.29	4.6XX–0 46X0–6 (66%) 46XY–3 (33.33%)
III	0.9	0.1	44	4.6	2.2	46XX–100%

Presenting complaint in group I along with primary amenorrhea include cyclical pain abdomen in 8 patients (23.5%) and dyspareunia and dysmenorrhea in 4 patients (11.7%), and 33 patients (98%) had breast development in stages III and IV. Axillary hair was present in 33 patients (98%), and pubic hair development was stage III and IV in 33 patients (98%). So the development of secondary sexual character was normal in group I (Table 2). In group II, secondary sexual characters were absent in all the patients, 1 patient presented with a mass per abdomen (11%) and 3 patients, i.e., 33.3% of the patients presented with hirsutism. Axillary hair was absent in 7 patients (77.7%) and present in 2 (22.2%) patients. In group III, i.e., hypogonadotropic group, there was only 1 patient, she presented with delayed development with primary amenorrhea and absent secondary sexual characters (Table 2).

In group I mean FSH, LH estradiol, prolactin and TSH values are 6.89 miu/mL, 8.8 miu/mL, 45 pg/mL, 20.8 ng/mL, and 3.05 iu/mL. In group II, mean values of FSH, LH, estradiol, prolactin, and TSH are 51.82 miu/mL, 13.3 miu/mL, 12.7 pg/mL, 22.1 ng/mL and 5.4 miu/mL (Table 3). Karyotyping in group I was 46XX for all patients, out of 33 patients in group I, 6 underwent a vaginoplasty, 10 (29.4%) underwent surgical management, 11 patients (32.3%) were managed medically, and 7 patients (20.5%) advised serial dilatation. In group II 6 patients had 45XO karyotyping, and 46XY was seen in 3 patients (33.3%). Out of the 3 patients with 46 XY karyotyping, gonadec-

Table 4: Management in each group

Group	Treatment
Group I	Vaginoplasty 6 (–17.64%)
	Surigical 10 (29.41%)
	Counselling 11(32.35%)
	Serial dilatation (20.5%)
Group II	Surgical 3(33.33%)
	Medical 6 (66.66%)
Group III	Medical 1(100%)

tomy was done in 2 patients and 1 patient presented with malignancy who underwent chemotherapy, patients with 46 XX karyotyping were managed medically. Group III patients were managed medically (Table 4).

DISCUSSION

In our study 77% of the patients were eugonadotropic, 20% were hypergonadotropic and 2% were hypogonadotropic, this is in comparison to Habiba Khatoon study in which eugonadotrophic were 72% , hypergonadotropic were 24% and Manee Rattan and Chaiyanont study, in which eugonadotropic was 47.6%, hypergonadotropic were 33% and hypogonadotropic were 12.8%.[5,6]

In group I presenting complaints in our study along with primary amenorrhea include pain abdomen in 23.5% and 2% presented with infertility, this is in comparison to Khatoon study where 2% had infertility, and 30% had pain abdomen.[5]

Mean FSH in our study in group I was 6.8 miu/mL, and group II was 51.82 miu/mL whereas in Habiba Khatoon study it was 4.1 miu/mL in group I and 46.62 miu/mL group II. Mean LH in our study in group I was 8.8 miu/mL and in group II was 13.3 miu/mL whereas in Habiba Khatoon study it was 7.7 miu/mL in group I and 40.5 miu/mL in group II.[5]

CONCLUSION

Patients and their parents presenting with primary amenorrhea need to be counseled regarding their menstrual, coital and reproductive outcomes. Primary amenorrhea is an extremely stressful situation for young girls and needs psychological counseling to prevent long-term sequelae. The feeling of defeminization and underdevelopment of secondary sexual characters is the major concern in patients and their parents, which have to be addressed with careful counseling.

In our study, MRKH is the most common cause of primary amenorrhea. Surgical management was required for agenesis of vagina and girls presenting with obstructive symptoms. Gonadectomy was required for hypergonadotropic group with the presence of the Y chromosome.

This study shows the importance of ascertaining the sex of the child in early age and karyotyping, as one patient in group II presented with stage 4 malignancy which could have been prevented by early gonadectomy.

Fertility concerns and other options of assisted reproductive techniques have to be discussed like surrogacy for patients with Mullerian agenesis, hormonal treatment with *in vitro* fertilization with donor oocyte for patients with gonadal dysgenesis and ovulation induction with gonadotropins for patients with hypogonadotropic amenorrhea.

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