

Primary Amenorrhea: Analysis of 108 Cases

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Abstract

Primary amenorrhea is defined as the absence of menses in females by the age of 14 years in the absence of secondary sex characteristics or the absence of periods by the age of 16 years regardless of appearance of secondary sex characters. A total of 108 cases of primary amenorrhea were referred to gynecological out-patient department of BIRDEM Hospital, Bangladesh between July 1995 to July 2008. These patients were studied with the aim to find out the cause of amenorrhea. After taking the detailed history, physical examinations and necessary investigations, patients were subjected to laparoscopic evaluation. The study highlights the role of transabdominal sonography in the work up of these cases and compare those with laparoscopic findings. About 69.4% of primary amenorrhoea were due to mullerian dysgenesis; 19.4% due to gonadal dysgenesis; 2.7% due to male pseudohermaphroditism with virilization; 2.7% due to genital tuberculosis and only one case was due to testicular feminization syndrome. Sonographic findings differ from laparoscopic findings in many cases. It can be observed that for optimal evaluation of primary amenorrhea, laparoscopy is the key tool for diagnosis.

Keywords: Primary amenorrhea, phenotypes, karyotyping, neovagina.

INTRODUCTION

Primary amenorrhea is defined as absence of menses in females by the age of 14 years in the absence of growth of secondary sexual characteristics.¹ It has been estimated that prevalence of primary amenorrhea in the college going women is 2.6 to 5%.²

Differential diagnosis of primary amenorrhea has long been an interesting intellectual exercise which has become more fascinating with the unfolding of knowledge of genetic and hormonal influence on the phenotyping development.³

It is one of the common problems in gynecological out-patient department. It has a number of etiological factors including sex chromosomal abnormalities. Pathological amenorrhea can result from disturbed function anywhere in hypothalamo-pituitary-ovarian-uterine axis with or without an associated organic lesion. In the present study we analyzed 108 cases of primary amenorrhea to find out the etiological factors behind and to determine the role of laparoscopy in the work up.

MATERIALS AND METHODS

This was a prospective hospital based clinical observational study from July 1995 to July 2008; one hundred eight cases of primary amenorrhea attended the gynecology out-patient department of BIRDEM hospital. All the patients were analyzed based on clinical evaluation including detailed history specially with regards to developmental parameters, anthropometric measurements, detailed examination of genitalia, confirming

presence or absence of vagina, uterus and ovaries. Two-dimensional USG of whole abdomen was done in all cases. Hormone assay, karyotyping and ovarian biopsy were done incases where thought relevant.

RESULTS

After a thorough clinical evaluation, the patients were classified in different categories of amenorrhea. Later confirmation of clinical findings were done by laparoscopy, ovarian biopsy and other biochemical tests. Patients were grouped according to cause of amenorrhea in Table 1.

Out of 108 cases, 101 patients were unmarried and rest were married. Primary infertility was complained by one married patient of group I and another married patient of group II. Breast development was poor in all the patients of group II and three

Table 1: Causes of amenorrhea

Group I	Eugonadotropic-78 (72%) <ul style="list-style-type: none"> • MRKHS-74 (68.5%) • Imperforate hymen-1 (0.93%) • Genital tuberculosis-3 (2.77%)
Group II	Hypergonadotropic hypogonadism-26 (24%) <ul style="list-style-type: none"> • Turner syndrome (3.7%) <ul style="list-style-type: none"> - Pure Turner-3 - Mosaic Turner-1 • 46 XX Gonadal dysgenesis-22 (20.4%)
Group III	Miscellaneous group <ul style="list-style-type: none"> • Hermaphrodites-4 (3.7%) • Male pseudohermaphrodite-3 (2.7%) • Testicular feminization syndrome-1(0.93%)

male pseudohermaphrodites of group III. Breast development was normal in group I patients and the patients of testicular feminization syndrome. Hirsutism was present in three patients who presented as pseudohermaphrodites. Aparunia was complained by the married patient of testicular feminization syndrome. The presenting complaints of the three groups of patients are given in Table 2.

Table 2: Presenting complaints in three groups of patients

	Group I	Group II	Group III
Primary amenorrhea	78	26	4
Primary infertility	1	1	0
Poor breast development	0	26	3
Hirsutism	0	0	3
Aparunia	0	0	1

All were phenotypically female. Shortest patient was in group II. Group III patients were taller than other groups. Stigmata of Turner syndrome was present in 4 patients. Patient of testicular feminization was a tall attractive woman. General physical characteristics are given in Table 3.

Axillary and pubic hair were normal in group I patients, sparse in group II and sufficient in 3 patients of male pseudohermaphrodites and was sparse in testicular feminization syndrome. Three male pseudohermaphrodites had hairy body and facial hirsutism. Genitalia was normal in group I patients, infantile in group II patients. In 2 patients with male pseudohermaphroditism genitalia was female type with significant cliteromegaly while in 1 patient labia was fused with cliteromegaly. Fused labia contained gonads. In the testicular feminization syndrome, external genitalia was female type with mild cliteromegaly.

In 71 patients of group I, vagina was practically absent and represented by a dimple of 2 to 3 cm depth. In 3 married patients of group I vagina was 6-7 cm in depth with a blind pouch, but no cervix. In 4 patients of group I normal vagina with cervix was present. Three patients were cases of genital tuberculosis and one patient had imperforate hymen. In group II vagina was present in full length with hypoplastic cervix in all cases. In 3 pseudohermaphrodites, only lower 1/3rd of vagina was present; in patient with testicular feminization syndrome a small vaginal pouch was present. Secondary sex characteristics of the patients are given in Table 4.

Prolactin and TSH level were normal in all groups. Hormone analysis was normal in group I patients. FSH and LH level was

high in group II patient; but estradiol level was low. FSH and LH level was high in group III patients except testicular feminization syndrome where it was at upper limit normal. Testosterone was low in 3 male pseudohermaphrodite patients and high in testicular feminization syndrome. In Table 5 results of hormone analysis are given.

Regarding size, presence or absence of uterus and presence and absence of ovaries laparoscopy could give better information than transabdominal sonography in group I patients, which constitute the majority of the patients of this study (78.72%). Transabdominal sonography could detect absent uterus only in 50 (64%) patients and hypoplastic uterus in 27 (30.75%) patients whereas laparoscopy showed uterus to be absent in 67 (85.9%) cases and hypoplastic uterus only in 7 (9%) patients. Ovaries were found to be absent in 5(4.63%) patients in transabdominal sonography but the figure was only 3 (2.78%) after laparoscopy. Two missed ovaries by transabdominal sonography were found by laparoscopy to be placed high up in lumber region. Table 6 shows comparison of findings between transabdominal sonography and laparoscopy. Chromosomal anomaly was found in 7 (7.4%) out of 108 patients. Karyotype was 46XX in group I patients and their gonadal biopsy showed primordial follicles. Karyotype was 45XO in 3 patients and 45XX-q in 1 patient and 46XX in 22 patients of group II. Their ovarian biopsy showed no primordial follicles. Karyotype was 46XY in all 4 patients in group III and their gonadal biopsy showed testicular structure. Results of karyotyping and gonadal biopsy are shown in Table 7.

DISCUSSION

The study was done to establish diagnosis of 108 cases of primary amenorrhea. Spectrum of pathological conditions is similar to other studies. Commonest cause of amenorrhea was anatomical (69.5%). Similar finding was reported by Rao and Pallai (50%)⁴ and by Kumar and Mittal (54.2%).⁵ In Bangabandhu Sheikh Mujib Medical University it was found to be 60%.⁶

Renal anomaly was present in 27 (25%) patients. In one study renal ectopy and agenesis has been reported in 34% and 47% respectively in patients with mullerian agenesis.⁷ Fore et al noted 15% incidence of renal ectopy in 39 patients of mullerian agenesis.⁸

In eugonadotropic cases 3 (2.77%) cases had genital TB which was diagnosed by laparoscopy and endometrial sampling. Incidence of tuberculosis in Rao and Pillai study was 2.5%⁴ and in Kumar and Mittal's study it was 6.3%.⁵

Table 3: General physical characteristics

Physical characteristics	Group I (78 patients)	Group II (26 patients)	Group III (4 patients)
Phenotype	Female	Female	Female
Height	Mean: 150.22 cm Range: 148-155 cm	Mean: 145.92 cm Range: 120-156 cm	Mean: 152 cm Range: 148-156 cm
Any special feature	-	Stigmata of Turner 4 (15.4%)	3 (75%) Rough muscular body 1 (25%) Tall attractive lady

Table 4: Secondary sex characters

Characteristics	Group I (78 patients)	Group II (26 patients)	Group III (4 patients)
Breast	T ₃ -T ₄	T ₁ -T ₂	T ₁ -T ₅
Axillary and pubic hairs	Normal female distribution	Sparse	Adequate 3 (75%) Sparse 1 (25%)
Hirsutism	Absent	Absent	Severe 2 (50%) Moderate 1 (25%) Absent 1 (25%)
Ambiguity of external genitalia	Absent	Infantile	**02(50%)—Female type with significant cliteromegaly **01(25%)—fused labia with micropenis **01(25%)—Normal female type with mild cliteromegaly
Vagina	*71 (91%)—2 cm *3 (3.85%)—6-7 cm *4 (5.1%)—Normal vagina with cervix	Present in all cases with hypoplastic cervix	3 (75%) lower 1/3rd 1 (25%) a small pouch

*Genotype: Female—46 XX

**Genotype: Male—46 XY

Table 5: Hormone analysis

	Group I	Group II	Group III
FSH	Mean: 4.17 mIU/ml Range: 2.50-7 mIU/ml	Mean: 46.62 mIU/ml Range: 30-80 mIU/ml	Mean: 37.75 mIU/ml Range: 38-42 mIU/ml TFS: 10 mIU/ml
LH	Mean: 7.72 mIU/ml Range: 6.05-9 mIU/ml	Mean: 40.50 mIU/ml Range: 23-80 mIU/ml	Mean: 47.00 mIU/ml Range: 40-63 mIU/ml TFS: 8 mIU/ml
Estradiol	Mean: 86.70 pg/ml Range: 65.50-120 pg/ml	Mean: 7.41 pg/ml Range: 50-14 pg/ml	TFS: 190 pg/ml
Testosterone	Not done	Not done	Mean: 0.85 ng/ml Range: 0.6-1.2 ng/ml TFS: 15 ng/ml

Table 6: Comparison of findings between transabdominal sonography and laparoscopy

Group I						
	UTERUS			OVARY		
	Absent	Hypoplastic	Normal	Absent	Streak gonad	Present
USG	50 (64%)	24 (30.75%) 2-3 cm	3 (3.85%)	5 (6.4%) 2-Bilateral 3-Unilateral	-	73 (93.6%)
Laparoscopy	67 (85.9%)	7 (9%) 2-3 cm	3 (3.85%)	3 (3.85%) Unilateral 2 Rt 1 Lt	-	74 (94.9%)

Table 7: Results of karyotyping and gonadal biopsy

	Group I (78 patients)	Group II (26 patients)	Group III (4 patients)
Karyotyping	46 XX	45 XO – (3) 45 XX – q –(1) 46 XX – (22)	46 XY (4)
Gonadal biopsy	Done only in few cases Primordial follicles present	- Stroma only - No primordial follicles	Typical structure of testes

Gonadal dysgenesis was present in 26 (24%) of patients in the present study. In the study of Rao and Pillai it was 23.5%⁴. Turner syndrome was found in 4 (3.7%) cases. It was 2.5% in the study of Rao and Pillai.⁴

Male pseudohermaphrodite containing XY-karyotype was seen in 4 (3.7%) patients in the present study. It was 7.5% in the study at Bangabandhu Sheikh Mujib Medical University.⁶ There was only one patient of testicular feminization syndrome. Very few cases of testicular feminization syndrome are reported in medical literature.^{9,10}

Patients were evaluated clinically, ultrasonographically and laparoscopically. A significant difference was found between ultrasonography and laparoscopy findings in group I patients which was mentioned earlier. Of the 4 pseudohermaphrodite patients testes were found in lateral pelvic wall in three patients and in labial fold in one patient which was proved by biopsy. Evaluation of primary amenorrhea by laparoscopy gives a better view of genital organs and facilitate taking biopsy from gonad. For gynecologist it is easy to do a laparoscopy and to give the prognosis immediately. So, for optimal evaluation of primary amenorrhea, laparoscopy is very useful investigation.

CONCLUSION

Patients with primary amenorrhea require special psychological counseling. These young girls will have major problem with future sexual activity and their fertility. Sexual problem can be solved by creating a neovagina at appropriate time either surgically or nonsurgically. Surgical correction of external genitalia and removal of gonads were done in male pseudohermaphrodites. Hormone therapy was given in patients with gonadal dysgenesis. Regarding fertility the result is hopeless

in almost all the cases in the context of our country where surrogacy and ovum donation is still not allowed.

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