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Adolescent Menstrual Problem in a Form of Primary Amenorrhoea-A Challenge to Gynaecologist

[1]Sabyasachi Ray, [2]Raj Sekhar Sarkar,
[3]Partho Mukhopadhyay and [4,5]Samiran Bisai

[1]Department of Obstetrics and Gynaecology,
Midnapore Medical College, Midnapore, West Bengal, India
[2]Department of Obstetrics and Gynaecology,
IPGME and R. / SSKM College and Hospital, Kolkata, West Bengal, India
[3]Department of Obstetrics and Gynaecology, Medical College, Kolkata, West Bengal, India
[4]Department of Anthropology, North Eastern Hill University, Shillong, Meghalaya, India
[5]Department of Anthropology, Vidyasagar University, Midnapore, West Bengal, India

Abstract: Adolescence of a woman is a transitional period between puberty and legal adulthood. At this milestone diagnosis of the etiology of primary amenorrhoea and managing the problem is a difficult task to a gynaecologist. A total of 31 adolescent girls aged 13-19 years with primary amenorrhoea was studied and followed up in the Department of Obstetrics and Gynaecology at IPGME and R, Kolkata, India. The detail history was obtained and physical examination with special importance to the development of secondary sexual characters was performed. All patients had been meticulously evaluated and treated with both medical and surgical approach. Results revealed that the mean (SD) age and height was 15.9±1.69 years and 1.34 ±0.08 m. Of the 31 primary amenorrhoea cases, 48.39 and 29.03% were due to anatomical defects and chromosomal disorders. While, 19.35% due to HPO axis defects and one case had Tuberculosis endometritis. It was noted that 89% patients with chromosomal disorder were of low height (<1.40m.). More importantly, one every third patients with anatomical defects started regular period (without hormone), 33.33% of patients with chromosomal defects started period but only with hormone therapy. In conclusion, a meticulous clinical evaluation followed by proper investigations can identify the etiology of maximum cases. Timely hormonal supplementation helps both to gain height to some extent and to develop secondary sexual characters. Regarding outcome as already mentioned, more scientific developments and their easy availability can improve the prospect in future. What is more important is the timely management and counseling regarding the options available.

Key words: Adolescent · Amenorrhoea · Mullerian · Karyotype · Turner syndrome · India

INTRODUCTION

Adolescence is the milestone of womanhood. Because a woman is not born as woman, she becomes woman with the attainment of reproductive maturity which starts with puberty or the beginning of adolescent. Of all the changes of puberty initiation of menstruation (menarche) is the most important. Amenorrhoea indicates in interruption of the complex inter relationship among these five factors are involved in the onset and continuation of normal menstruation: (1) Anatomical patency of genital tract, (2) Normal female chromosomal pattern, (3) Normal Hypothalamo-Pituitary-Ovarian axis, (4) Responsive endometrium and (5) Active support from other endocrine glands e.g. Adrenal and Thyroid.

Primary amenorrhoea is defined as absence of initiation of menses by the age of 14 years in the absence of secondary sexual characters, or by the age of 16 years in presence of secondary sexual characteristics [1]. It was well documented that, in Kolkata the median age at menarche of 12.0 years amongst well-nourished school girls [2].

Corresponding Author: Samiran Bisai, Department of Anthropology, Vidyasagar University, Midnapore - 721102, West Bengal, India. E-mail: samiranbisai@yahoo.com.

Few problems in gynaecology are as challenging and taxing to the gynaecologists as primary amenorrhoea. Even the diagnosis, investigations and management options of primary amenorrhea are well established. It may be the first obvious sign of an abnormality of both reproductive and non-reproductive system.

The etiology of primary amenorrhoea continues to be an interesting and intellectual exercise that has become more fascinating with the unfolding of knowledge of genetic and hormonal influences on phenotypic development. Worldwide gonadal dysgenesis is the commonest cause of primary amenorrhoea and Mullerian development disorders and Androgen insensitivity syndrome are second and third commonest, respectively [1].

Given the above context, the present study was conducted to investigate the etiology of primary amenorrhea adolescent girls in Kolkata, West Bengal. The management options and outcomes were analysed.

MATERIALS AND METHODS

The present study was conducted among the patients attending the out-patient department of the department of Gynaecology and Obstetrics in the Institute of Post Graduate Medical Education and Research (IPGMER) and SSKM Hospital, Kolkata over a period of one year from January 2004 to April 2005. A total of 31 adolescent girls aged between 13 to 19 years were included. The detail history was obtained and physical examination with special importance to the development of secondary sexual characters was performed. The following investigations were performed. These are routine hemogram, blood sugar, renal function tests, Liver function tests, urine analysis, hormonal studies - FSH, LH, Thyroid status, prolactin, testosterone as needed and ultrasonography. CT scan and MRI were advised selectively to those patients who had low FSH. Karyotyping was also not available at this centre, so buccal smear for Barr bodies were used as cytogenetic evaluation in majority of cases. Intravenous pyelography was also performed in selected cases of Mullerian development disorder and in some cases chromosomal defects. The study protocol was approved by the respective institutional ethical committee prior initiation of the study. As well as study objective was discussed and consent was obtained from the patients and guardian before inclusion of the study. Height was measured and recorded using anthropometer to the nearest 0.01 m. The mean and standard deviation of age and height was calculated using MedCalc statistical software.

After investigations, treatment as well as counseling was provided to all patients. Surgery sometimes supplemented by hormonal therapy was the mainstay of treatment for the patients with anatomical defects, whereas hormonal supplementation was the mainstay of management for other patients. One patients with severe hyperprolactinemia were given Cabergolin. Few patients were advised for follow up without any definite treatment especially a patient with Ebstein anomaly.

Result Analysis: A total of 31 patients aged between 13-19 years were included in the present study. The mean (SD) age was 15.9 ± 1.69 years. Twenty (64.52%) of them were 16 years or below and 11 (35.48%) patients were older than 16 years. Three (9.68%) of them were married at the time they presented.

The majority of the patients presented with amenorrhea as a main complaint, except for 3 whose main complaint was cyclical abdominal pain. One patient had complained of swelling in the inguinal region, 13 patients of them had complain of hypogonadism i.e. no/ill development of breast, absent or minimum of pubic and axilary hair.

The etiologies of these patients could be divided in the following categories: Majority of the patients (48.39%) had anatomical defects, 9 patients (29.03%) had chromosomal defects, 6 patients (19.35%) had hypothalamo-pituitary-ovarian (HPO) axis defects (hypogonadotrophic hypogonadism) and 1 patient had TB endometritis (Table 1). In anatomical defect - 10 had Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH syndrome) or its variants, 2 had imperforate hymen and 3 had transverse vaginal septum. In chromosomal defects - 1 patient had 45XO (Turner's syndrome) and 3 had Turner's mosaicism. In the rest of the patients though Karyotyping could not be performed but Sex-chromatin study revealed either absent or very scanty Barr body. One patient gonadal biopsy revealed testicular tissue in maturation arrest. In H-P-O axis defect cases - 1 patient had hyperprolactinaemia due to a pituatory adenoma. Her period ultimately started after treatment with Cabergolin for 7-8 months; one patient in this group had Ebstein anomaly and features of delayed puberty. Secondary sexual characters development of all the patients at the time of presentation is given in table 1. It was noted that majority of the patients with chromosomal defects had absent or minimal secondary sexual character development.

Table 1: Secondary sexual characters development of all the patients at the time of presentation.

	Breast (Tanner's stage)					Pubic hair (Tanner's stage)					Axillary hair		External genitalia	
Type of defects	I	II	III	IV	V	I	II	III	IV	V	Present	Absent	Infantile	Normal
Anatomical	0	2	10	3	0	0	8	6	1	0	14	1	0	15
Chromosomal	6	2	1	0	0	8	1	0	0	0	1	8	3	6
H-P-O axis	1	4	0	1	0	3	2	1	0	0	1	5	3	3
Others	0	0	1	0	0	0	1	0	0	0	1	0	1	0
Total	7	8	12	4	0	11	12	7	1	0	17	14	7	24

Table 2: Distribution of height of adolescents according to their abnormalities.

Height (cm)	Anatomical	Chromosomal	H-P-O Axis	Others	Total
<140	3	8	4	0	15
140-144	7	0	1	0	8
145-149	3	0	0	0	3
=150	2	1	1	1	5
Total	15	9	6	1	31

Table 3: Treatment given to the patients according to their problem.

	Medical					Surgical			
Type of defects	Hormonal	Non-hormonal	Both	Hymenectomy	Excision of Transverse vaginal septum	Vagino plasty	Metro plasty	Others	Expectant and counseling
Anatomical	1	0	0	2	3	1	0	1	7
Chromosomal	9	0	0	0	0	0	0	0	0
H-P-O axis	0	0	2	0	0	0	0	0	4
Others	0	0	0	0	0	0	0	0	1
Total	10	0	2	2	3	1	0	1	12

The mean (SD) height of studied subjects was 1.34 ±0.08m. It was observed that the majority of the patients were below <1.45m (Table 2). This is especially for chromosomal defects group. It had been noted that about 89% patients (8 out of 9) with chromosomal disorder were of low height (< 1.40 m.).

By clinical evaluation and also by USG and Laparoscopy it was noted that excepting 1 patient where uterus was bulky due to cryptomenorrhoea the uteruses were either nodular or infantile in all cases of anatomical defect. Of the 15 patients with anatomical defects, 2 had imperforate hymen and 3 had transverse vaginal septa but ovaries are normal.

Uteruses and ovaries were hypoplastic in majority of cases of chromosomal defect; absent in 1 where there were inguinal gonads which later on proved to be testis after biopsy. In H-P-O axis defect group uterus or ovaries were either hypoplastic or normal. One patient with MRKH syndrome had horseshoe shaped kidney and another had hydronephrotic and hydroureteric changes.

Due to non-availability of Karyotyping at this centre and as most of the patients could not afford it from outside; sex-chromatin study was done in all patients. In chromosomal group they were absent in 2 patients and very scanty in another 7 patients. It was normal in rest of the patients, 5 out of 9 patients with chromosomal defect group could afford to do Karyotyping - 1 normal 46XX, 1 Turner's 45XO pattern and rest 3 had 46XX/45XO mosaic pattern.

In hormonal study 8 out of 9 patients of chromosomal defect group had increased level of FSH, LH, TSH, Prolactin and low Testosterone level (Table 3). 1 patient had normal FSH increased LH, normal TSH and Prolactin but increased Testosterone (near normal male) level - this patient later proved to be a case of Androgen Insensitivity Syndrome (AIS). 1 patient with H-P-O axis defects had hyperprolactinemia and 1 also had incidental hypothyroidism.

Operative treatment was the mainstay of treatment for anatomical defects group; sometimes hormonal supplementation was also required. In rest of the cases

Table 4: Outcome of the patients after treatment.

	Menstruation		
		Occurred	
Type of defects	Not Occurred	With Hormone	Without Hormone
Anatomical	10	0	5
Chromosomal	6	3	0
H-P-O axis	4	2	0
Others	1	0	0
Total	21	5	5

including the patient with TB of the endometrium hormonal supplementation was main treatment.

Table 4 shows that only 33.33% of patients with anatomical defects started regular period without hormone, 33.33% of patients with chromosomal defects started period but only with hormone and 33.33% of the H-P-O group started period (1 after correction of hyperprolactinemia and others with hormone). However, conception was not evaluated due to short study period.

DISCUSSION

The main role of gynaecologist in a case of primary amenorrhoea is to identify the etiology and plan the management. Though as per the accepted definition the age limit has been quoted as 14 and 16 years, respectively as already mentioned. Rokade and Mane [3] found in India the mean menarcheal age of adolescents was 12.62 ± 1.05 years and in Kolkata the median age at menarche among well nourished girls was 12.0 (range 10.0 - 16.0) years [2].

Lancet [4] stated that height of less than 1.45 m as static features of Turner's syndrome. In this study, 88.89% of patients in chromosomal defect group had height <1.45 m excepting one who later proved to be a case of AIS. Patients with turner's mosaic and/or unknown karyotype usually do not have the stigmata of Turner's syndrome and attain normal height. But, in Indian perspective the average height of adolescents girls is less than 1.45 m supported by Maliye *et al.* [5] where the mean height of the adolescent Indian girls was found to be 1.43 m in the same age group.

In this study the commonest etiology of primary amenorrhoea was anatomical defects. Similarly, Rasool *et al*. [6], Kumar and Mittal [7], Rao and Pilai [8], Mondal *et al*. [9], Jabbar [10] in their study also found more prevalence of anatomical defects than chromosomal disorders or gonadal dysgenesis.

Gupta [11] reported in his study more prevalence of genital TB (13%) among 47 cases of primary amenorrhoea. Because of the reduction of the incidence of tuberculosis we found only one case in the present study.

Though different treatment modalities are available but outcome regarding regular menses and fertility potential is not so satisfactory. With continuing advancement of technologies of artificial reproduction there is still hope for some patients with primary amenorrhoea to have their genetic offspring [12-14]. But these facilities are expensive and not easily available. What is more important is the proper counseling to the patient and her relatives.

In conclusion primary amenorrhoea is a challenge to the treating gynaecologist. A meticulous clinical evaluation followed by proper investigations can identify the etiology in a large number of cases. Timely hormonal supplementation helps both to gain height to some extent and to develop secondary sexual characters. Operative treatment, often only creation of a vaginal canal of adequate depth helps a lot. Regarding outcome as already mentioned, more scientific developments and their easy availability can improve the prospect in future. What is more important is the timely management and counseling regarding the options available.

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