

Frequency of Primary Amenorrhea and the Outcome of Treatment at Liaquat University Hospital

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ABSTRACT

OBJECTIVE: To determine the frequency of primary amenorrhea and to enlist etiological factors and outcome of treatment of primary amenorrhea.

DESIGN: A descriptive case series.

SETTING: Department of Obstetrics and Gynaecology (Unit-II) Liaquat University Hospital Hyderabad, Sindh – Pakistan, from January 2006 to December 2007.

METHODS: All patients presenting with primary amenorrhea were included in the study and patients having secondary amenorrhea including pregnancy were excluded. All the data collected by history, examination and investigations were recorded on a proforma. Data were analyzed using SPSS version 10.0.

RESULTS: Total number of patients admitted was 2,505. Frequency of primary amenorrhea was 0.75%. Imperforate hymen was found in 21.05% cases, pure gonadal dysgenesis in 15.7%, constitutionally delayed puberty in 10.52%, hyperprolactinemia in 10.52%, polycystic ovaries in 5.26%, Turner's syndrome in 10.52% and testicular feminization in 10.52% cases. Patients with constitutionally delayed puberty had spontaneous onset of menstruation. Outcome was good in all patients with cryptomenorrhea. Two of them got married and conceived successfully. The patients with primary amenorrhea due to polycystic ovaries and hyperprolactinemia had resumption of normal menstruation after medical therapy. In patients with testicular feminization, testicular tissue was removed and estrogen/progestogen therapy was given.

CONCLUSION: Primary amenorrhea is one of the important reasons for distress of family and patient herself. Literature review has shown that low frequency and fear of exposure of defect may be the reason for not seeking medical advice. In our setup too, these observations were found. Patient awareness and the proper counseling of parents regarding the treatment options available and need for follow up can help in deciding the sex of rearing and even restoring the fertility in many of these women.

KEY WORDS: Primary amenorrhea. Frequency. Causes. Follow up. Outcome.

INTRODUCTION

Primary amenorrhea is defined "when there is failure to menstruate by age 16". Menstruation may normally occur at any time between 10-18 years of age.¹ It is more useful to look upon secondary sexual characteristics, and failure of development of any secondary sexual characteristics by the age of 14 years should be investigated. Ross proposed that primary amenorrhea should be investigated if sexual infantilism persists until the chronological age of 16 or if irrespective of normality of secondary sexual characteristics menstruation has not occurred by the age of 18.² Shearman suggested that if normal menstruation has not begun within 2 years of onset of an otherwise normal puberty, then congenital absence of the uterus / vagina should be excluded if this has not previously been clinically detected.³ If puberty is inappropriate e.g. virilizing or if abnormal gonadal tissue has been detected prior to puberty, then in time complete inves-

tigations are mandatory earlier in time.⁴ Causes of primary amenorrhea are hypergonadotrophic hypogonadism, hypogonadotrophic hypogonadism, eugonadotrophic and virilizing amenorrhea. Among central nervous system disorders, Kallmann's syndrome is a familial syndrome of sexual immaturity and insomnia or hyposmia associated with midline cranial defects the primary abnormality is hypothalamic dysfunction with impairment of release of gonadotrophins.⁵ Laurence Moon Biedl syndrome is a recessive disorder, which has the clinical features of retinal dystrophy, truncal obesity. This is the likely result of consanguinity.⁶ Turner's syndrome (45 XO) occurs in one out of 2500 to 3000 patients. These patients have streak gonads, usually short with associated somatic abnormalities and eye defects like segmental iridogonidysgenesis without glaucoma.⁷ Among congenital abnormalities of the female genital tract, a non-functional uterus with uterovaginal agenesis (Mayer Rokitansky – Kuster – Hauser Syndrome) being one of the most

frequent causes of primary amenorrhea.⁸ It can sometimes be associated with renal agenesis or other renal abnormalities.⁹ Anorexia nervosa is primarily psychological disorder, it manifests by hypothalamic dysfunction. It is associated with amenorrhea and weightloss greater than 25 percent of ideal body weight. It is most common in white, middle to upper class success achievement oriented females.¹⁰ Anorexia nervosa, extreme exercise, eating disorders and celiac disease are the acquired causes of primary amenorrhea.¹⁰⁻¹⁵ This study will provide an insight into the frequency of cases, their causes and complications which may help to chalk out a management plan for primary amenorrhea.

MATERIALS AND METHODS

This study was carried out over a period of 2 years from January 2006 to December 2007 in the Department of Obstetrics and Gynaecology (Unit-II), Liaquat University Hospital Hyderabad. On admission, a detailed history was taken regarding family history of genetic abnormalities, birth, growth, development, nutritional and dietary factors, systemic diseases, previous surgeries, prior to diagnostic studies and results. After proper informed consent these patients were thoroughly examined as detailed history does not contribute as much to evaluation as does a careful physical examination. Patients and family members were reassured regarding the confidentiality of the data obtained from them. General physical examination was done to note the appearance, height, nutritional status, secondary sexual characteristics (Breast and areolar development, pubic and axillary hair) acne, hirsutism, visual fields and galactorrhea. Detailed systemic examination was made. Abdominal examination was performed to see any lower abdominal mass, hernia or any other abnormality. Pelvic examination was done to see the external genitalia (female or male), clitoromegaly, imperforate hymen, transverse vaginal septum, absent or blind ending vagina, presence and absence of uterus and cervix.

Inclusion Criteria

All the patients having primary amenorrhea were included in the study.

Exclusion Criteria

Patients having secondary amenorrhea including pregnancy were excluded from the study.

Rectal examination was done in few of the unmarried girls with absent vaginal to note the presence or absence of uterus and cervix. After taking a detailed history and thorough examination, these patients were investigated. Investigations performed were baseline (blood complete picture, urine analysis, random blood sugar, blood group) and specific including buccal

smear, for Barr bodies karyotyping, hormonal assays (Serum FSH, LH, T3, T4, TSH, prolactin, estrogen, progesterone and androgens), pelvic ultrasound, laparoscopy, X-ray wrist and metacarpal bones, X-ray skull and CAT Scan brain. All data were recorded on a predesigned proforma and were analyzed through SPSS version 10.0. Thoughtful counseling was provided to all patients. Purpose was to help out the patients for adjustment in the society in accordance with the gender most appropriate. These patients were followed up in the out patient department.

RESULTS

Total number of patients admitted was 2,505, among them, 19 patients presented with primary amenorrhea hence, incidence was (0.75%) in our unit. Patients presenting with primary amenorrhea were of age ranging from 12-30 years. Majority of them was of age group 16-20 years (**Table I**). Breasts were developed in 57.89% cases, infantile in 42.10%, while pubic and axillary hair were well developed in 68.42% of cases, and were scanty in 31.57% of cases. External genitalia were normal in 52.63% cases, were poorly estrogenized in 42.10% cases and ambiguous in 5.26% cases (**Table II**). Among 19 patients, height was less than 100 cms in 5.26% cases, between 100-125 cms in 15.78% and between 126-150 cms in 78.94% cases (**Table III**). Weight of these patients was between 40-45 kg in 15.78% cases, between 46-50 kg in 31.57%, between 51-55 kg in 26.31%, between 56-60 kg in 15.78% cases and more than 60 kg in 10.52% cases (**Table IV**). On chromosomal analysis, buccal smear was positive for Barr bodies in 73.68% cases and negative in 26.31% cases. Karyotyping was XO in 10.52% cases, XX in 73.68% and XY in 15.78% cases (**Table V**). On hormonal assays, follicle stimulating hormone level was found raised in 5 patients, it was low in 2 patients and was normal in 12 patients. Leutinizing hormone level was raised in 3 patients and was normal in 15 patients. Prolactin level was raised in 2 patients and was normal in 17 patients. FSH: LH ratio was raised in 1 patient of polycystic ovarian syndrome. In 19 patients of primary amenorrhea, two were diagnosed as cases of constitutionally delayed puberty. They were reassured. They had spontaneous resumption of menstruation after 2 years. Two of these got married and conceived successfully. Four patients were found to have cryptomenorrhoea due to imperforate hymen, and hymenectomy was performed in these patients. Three were diagnosed as a case of gonadal dysgenesis. They were given estrogens and progestogen in the form of tablet proglyuton (estrodial valerate 2mg, Norgestrel 0.5mg) 1 tablet daily. There was improvement in the development of secondary sex characters. Therapy was continued for 2 years

after which they did not come for follow up. In one patient vaginoplasty was performed to facilitate the sexual intercourse. One married patient out of 19 presenting with primary amenorrhea had association with polycystic ovaries. She was prescribed tablet duphaston (dydrogesterone) 10 mg twice a day for 10 days for 2 cycles, for withdrawal bleeding. Induction of ovulation was done with clomiphene for 3 cycles. She was advised reduction of weight and conceived after 3 cycles of clomiphene therapy. Two patients presented with primary amenorrhea in relation to hyperprolactinemia but had no evidence of prolactinoma. They had regular menstrual cycles on bromocriptine therapy 2.5mg twice a day for three to six months. In patients with testicular feminization, testicular tissue was removed and estrogen progestogen therapy in the form of tablet progyluton (estradiol valerate 2mg, norgestrel 0.5mg) was given. These patients were lost to follow-up. Most patients with primary amenorrhea came for follow up and outcome was good, except 3 patients with gonadal dysgenesis.

**TABLE I:
DISTRIBUTION OF CASES BY AGE (n=19)**

Age in years	No. of Patients	Percentage
10 – 15	02	10.52%
16 – 20	09	37.36%
21 – 25	03	15.78%
26 – 30	05	26.31%

**TABLE II:
DISTRIBUTION ACCORDING TO DEVELOPMENT**

Sec. Sex characters	Infantile		Well developed	
	No. of Patients	Percentage	No. of Patients	Percentage
Breasts	8	42.10%	11	57.89%
Pubic hair	6	31.57%	13	68.42%
Axillary hair	6	31.57%	13	68.42%
External Genitalia				
External Genitalia	No. of Patients		Percentage	
Normal	10		52.63%	
Poorly oestrogenized	8		42.10%	
Ambiguous	1		5.25%	

**TABLE III:
DISTRIBUTION OF CASES BY HEIGHT**

Height	No. of Patients	Percentage
Less than 100 cm	1	5.26%
100 – 125 cm	3	15.78%
126 – 150 cms	15	78.94%

**TABLE IV:
DISTRIBUTION OF CASES BY WEIGHT**

Weight in Kg	No. of Patients	Percentage
40 – 45 kg	3	15.78%
46 – 50 kg	6	31.57%
51 – 55 kg	5	26.31%
56 – 60 kg	3	15.78%
> 60 kg	2	10.52%

**TABLE V:
DISTRIBUTION OF CASES ACCORDING TO CHROMOSOMAL ANALYSIS**

Chromosomal	No. of Patients	Percentage
1. Buccal smear for Barr bodies		
- Positive	14	73.68%
- Negative	5	26.31%
2. Karyotyping		
- X0	2	10.52%
- XX	14	73.68%
- XY	3	15.78%

DISCUSSION

Primary amenorrhea creates problems such as social, psychosexual, infertility, osteoporosis and genital atrophy. Whenever a child presents with her parents and concern is expressed about her well being, it is important to record history and examination and then to institute the appropriate diagnostic investigations. However, a thorough physical examination is extremely important to identify the presence or absence of secondary sex characteristics. It is important to realize that normal breast development indicates either normal ovarian production of estrogens or peripheral conversion of androgen to estrogen. It is unlikely that full breast development will occur from peripheral conversion, thus the presence of secondary sexual characteristics is extremely important in evaluating patients for investigation.¹⁶ The frequency of primary amenorrhea was 0.75% out of 2,505 patients at our set up, which is the single tertiary care hospital receiving patients from all over the interior Sindh. This was the

reason for high frequency. It was different from the study done by Asifa Ghazi at Dow Medical College and Civil Hospital Karachi in 2004, where the frequency of primary amenorrhea was 0.065% among 19,900 cases.¹⁶ The frequency was low because Karachi is a large city with many tertiary care hospitals. The most frequent cause of primary amenorrhea in this study was imperforate hymen (21.05%), this was similar to the study done by Farhat Iqbal at King Edward Medical College in March 2003, in which they found 19.3% cases of imperforate hymen. Our study was also in contrast to the study done by Asifa Ghazi in 2004 at Dow Medical College where she found 46.15% cases due to anatomical defects among 13 patients of primary amenorrhea. In this study, 15.78% patients were diagnosed as having pure gonadal dysgenesis and this incidence was in contrast to the study done by Farhat Iqbal in 2004 where 3.8% had gonadal dysgenesis. In our study incidence of testicular feminization was 10.52% and similar was the incidence of Turner's syndrome (10.52%), however, it was high in the study of Asifa Ghazi where Turner's syndrome was found in 30.78% patients. Most of the patients in our study belonged to the age group 16-20 years (47.36%), this was in contrast to the study of Farhat Iqbal where 76.9% of patients presented between 15-25 years of age.¹⁷ Karyotyping is one of the fundamental investigations in the evaluation of primary amenorrhea. It was abnormal in 10.52% patients, which is in contract to the study done by Rajanjam in 2007 where he found chromosomal abnormalities in 34.57% patients. In another study done in China by Kong H et al, he found 17 cases of primary amenorrhea and 7 revealed a 46 XX Karyotype, 10 (158.8%) had abnormal Karyotype, 3 cases of 46 XY and 2 cases of Turner's syndrome.¹⁸ In our study among 19 patients, premature ovarian failure was not diagnosed as a cause of primary amenorrhea however, few cases of primary amenorrhea due to premature ovarian failure have been reported in other studies.¹⁹ There were no incidental findings.

CONCLUSION

Primary amenorrhea is an extremely stressful problem for a young girl and her parents. The clinician should handle the case with great sensitivity. Psychologic support can prevent long term sequelae. Counseling is of great importance in the management of cases of primary amenorrhea.

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