

# Causes of Primary Amenorrhoea among Patients Presenting at Aziz Fatimah Hospital Faisalabad

Zonia Tanveer Nizami<sup>1</sup>, Aalia Jadaan<sup>2</sup>

Assistant Professor<sup>1,2</sup>, Department of Obstetrics & Gynecology, Aziz Fatimah Trust Hospital and Medical and Dental College, Faisalabad

**Corresponding Author:** Dr. Aalia Jadaan, Department of Obstetrics & Gynaecology, Aziz Fatimah Trust Hospital and Medical and Dental College, Faisalabad.

Email: dr.aaliafarhan@gmail.com

## Abstract

**Objective:** to investigate cause of primary amenorrhoea among patients presenting at Aziz Fatimah Hospital, Faisalabad.

**Study Design:** descriptive cross sectional study.

**Duration of Study:** the study was conducted in Department of Obstetrics & Gynecology, Aziz Fatimah Trust Hospital and Medical and Dental College Faisalabad, for a duration of 1 year from May, 2014 to April 2015.

**Methodology:** fifty six patients presenting with primary amenorrhoea were enrolled for the study after history, examination and necessary investigations. The patients of age 16 to 40 years who never had menstruation in life were included in this study. Patients with surgical causes of amenorrhoea and secondary amenorrhoea were excluded from the study. All the required information was recorded on a predesigned Performa.

**Results:** the mean age of group was  $19.46 \pm 3.54$  years. Majority of the patients 37(66.07%) had height in the range of 126-150cm and 6 (10.71%) patients had height less than 100cm. Weight of main bulk (35.71%) of patients was 46-50 kg.

In this sample 21 (37.50%) patients had infantile breast development, the pubic hair was infantile in 20 (35.71%) patients and axillary hair was infantile in 17 (30.36%) patients. It was found that main causes of the amenorrhoea in these patients were related to anatomical defects in 25 (44%) patients. Followed

**Authorship Contribution:** , conceptualized study design, Data Analysis , <sup>3</sup>literature review, discussion, conclusion writing

**Funding Source:** No funding.

**Conflict of Interest:** No Conflict.

by chromosomal defects which were found in 17 (31%) patients and Hypothalamic-pituitary-ovarian (HPO) axis defects were recorded in 10(18%) patients. In 4 (7%) patients some other defects (like TB endometritis) were noted.

**Conclusions:** 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.

**Key words:** primary amenorrhoea, anatomical defects, chromosomal defects, kuster-hauser syndrome.

## Introduction

The phase connecting puberty and adulthood is termed as adolescence. In this transitional period there might be some complications like primary amenorrhoea, which are difficult to diagnose. It is a challenging situation for gynaecologist to discover the aetiology of primary amenorrhoea and its management.<sup>1</sup>

The absence of commencement of menses by the age of 14 years along with deficiency of secondary sexual characters, or by the age of 16 years in presence of secondary sexual characteristics is termed as primary amenorrhoea. It is responsible for connecting the series of events i.e. thelarche, pubarche, and menarche that expresses the puberty in adolescents' lives. Amenorrhoea can be a consequent of diverse ailments. Anomalies of the hypothalamic axis, blockades in outflow tract and gonadal dysgenesis are some important aetiological factors which are responsible for amenorrhoea. There are complex interactions between the hypothalamic pituitary axis, the ovaries and the outflow tract in the normal menstrual cycle.

Any disturbance in this complex and very structured categorization of events, or functional abnormalities in the hypothalamic pituitary ovarian axis can results

into abnormal menstruation or amenorrhoea. Amenorrhoea can be an endocrinological disease or can also be caused by structural abnormalities of the outflow tract.<sup>2,3</sup> From previous researches it was noted that about 40% causes are related to endocrine disorders in primary amenorrhoea. The causes responsible for secondary amenorrhoea can also be a cause for primary amenorrhoea. The secondary amenorrhoea is defined as nonappearance of menstruation for at least six months.<sup>4</sup>

It has been estimated that prevalence of primary amenorrhoea in the college going women is 2.6 to 5%. The diagnosis of primary amenorrhoea has long been an interesting intellectual exercise. It is becoming more captivating due to increase in knowledge of genetic and hormonal influence on the phenotyping development.<sup>5</sup> It has been noted that girls with poorly controlled or undiagnosed 21-OH deficient form of congenital adrenal hyperplasia can have delayed puberty.<sup>6</sup>

Anorexia nervosa which is a primarily psychological disorder and is confirmed by hypothalamic dysfunctions is accompanying with amenorrhoea and weight loss of more than 25% of ideal body weight.<sup>7,8</sup> There are some adapted causes of primary

amenorrhoea like intense exercise, eating disorders, anorexia nervosa and celiac disease.<sup>9-12</sup>

In our society primary amenorrhoea is an important reason for distress of family and patient having this condition. It has been found from previous researches that due to apprehension of disclosure of defect, women do not go for medical help. Proper counseling and awareness of the patient about the available treatment options are the key points for deciding the sex of rearing.<sup>13</sup>

## Methodology

This cross sectional study was started after taking approval from the hospital ethical committee. The patients were enrolled from the outdoor Department Of Obstetrics and Gynecology, in Aziz Fatimah Trust Hospital and Medical and Dental College, Faisalabad. The patients were enrolled for the study after history, examination and necessary investigations. The patients of age 16 to 40 years who never had menstruation in their life were included in this study. Patients with surgical causes of amenorrhoea and secondary amenorrhoea were excluded from study.

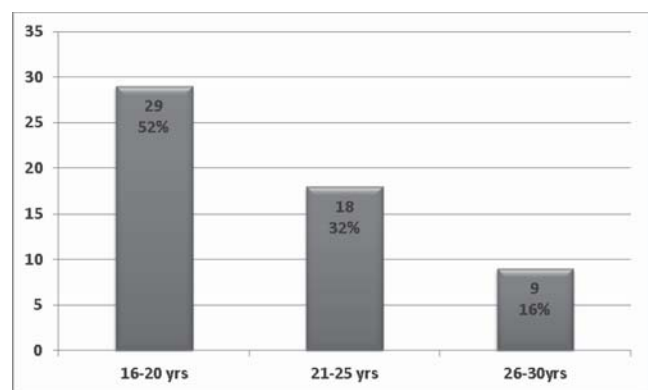
Participants were briefly described the objective of study and written informed consent was taken. Patients were given withdrawal bleed challenge, and who failed to bleed after progesterone challenge test were included in study. General physical examination was done to note the appearance, height, and nutritional status, secondary sexual characteristics including breast and areolar development, pubic and axillary hair. Abdominal examination was performed to see any lower abdominal mass, hernia or any other abnormality. Detailed 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.

Blood complete picture, urine analysis, random blood sugar and blood group, were done. Other investigations including buccal smear, karyotyping, hormonal assays, Serum FSH, LH, T3, T4, TSH, prolactin, oestrogen, progesterone and androgens were also done. Ultrasonography and laparoscopy was performed to visualize any pathology regarding the uterus and ovaries like any mass and absent or streak like ovaries. All data were recorded on a predesigned Proforma and were analyzed through SPSS version 16.

## Results

In this cross sectional study a total of 56 patients of primary amenorrhoea were selected during the study period. The mean age of this group was  $19.46 \pm 3.54$  years with maximum patients of age between 16-20 years followed by 21-25 years as shown in figure 1.



**Figure 1: Distribution of age of the patients**

According to the height distribution majority of the patients 37(66.07) had height range of 126-150cm and 6 (10.71%) patients had height less than 100cm. Weight of main bulk (35.71%) of patients was 46-50

kg and 40-45kg in 11 (19.64%) patients. Only 4 (7.14%) patients had weight more than 60 kg as given in table I.

**Table I. Distribution of Height and Weight**

Height in cm	Frequency of Patients	Percentage
< 100 cm	6	10.71%
100 – 125 cm	13	23.21%
126 – 150 cm	37	66.07%
Weight in Kg		
40 – 45 kg	11	19.64%
46 – 50 kg	20	35.71%
51 – 55 kg	13	23.21%
56 – 60 kg	8	14.29%
> 60 kg	4	7.14%

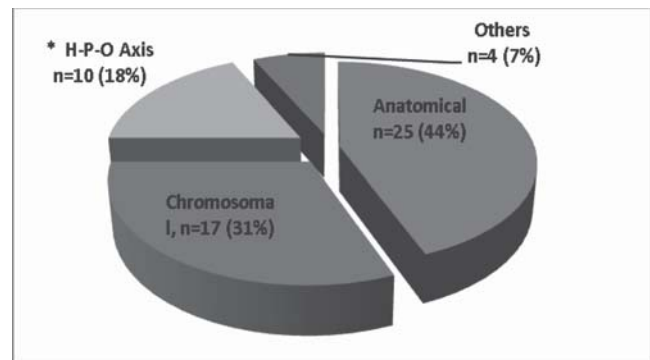
In this sample 21 (37.50%) patients had infantile breasts development and 35 (62.35%) had well developed breasts. The pubic hair was infantile in 20 (35.71%) patients and it was well developed in 36 (64.29%) patients. The axillary hair was infantile in 17 (30.36%) patients and was well developed in 39 (69.64%) patients as elaborated in table II.

**Table II. Distribution of Secondary Sex characters and External Genitalia**

Secondary Sex characters	Infantile	Well developed
	No. of Patients (%)	No of Patients (%)
Breasts	21(37.50%)	35(62.50%)
Pubic hair	20(35.71%)	36(64.29%)
Axillary hair	17(30.36%)	39(69.64%)
External Genitalia		
	No. of Patients	Percentage
Normal	24	42.86%
Poorly oestrogenized	28	50.00%
Ambiguous	3	5.26%

When the aetiologies of these patients were studied, it was found that main causes of the amenorrhoea in

these patients were related to anatomical defects in 25 (44%) patients. Followed by chromosomal defects which were found in 17 (31%) patients and Hypothalamic-pituitary-ovarian (HPO) axis defects were recorded in 10(18%) patients under study. In 4 (7%) patients some other defects (like two patients had TB endometritis, and two patients who could not be properly diagnosed for cause of amenorrhoea were also noted, shown as others in figure 2.



**Figure 2. Distribution of main causes of amenorrhoea**

\* Hypothalamo-pituitary-ovarian (HPO) axis defects

The anatomical defects included Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH syndrome) or its variants in 15 patients, in 4 patients imperforate hymen was seen and in 6 patients transverse vaginal septum was present. In the patients in whom chromosomal defects were seen it was noted that 4 had 45XO (Turner's syndrome) and 7 had Turner's mosaicism. Testicular tissue in maturation arrest was seen in two patients on results of gonadal biopsy. In the patients in whom HPO axis defect were found 4 patients had hyperprolactinaemia due to a pituitary adenoma. Ebstein anomaly and characteristics of deferred puberty were noted in another 4 patients.

The frequency of chromosomal abnormalities was found in 17 (31%) in primary amenorrhoea patients. Four main types of chromosomal abnormalities were detected. The numerical abnormalities of the XO chromosome in 8 (47 %) patients, structural abnormalities of the X chromosome in 4 (23.53%), mosaicism of X chromosome in 3 (17.6%) and male karyotype 46, XY was present in 2 (11.76%) patients.

## Discussion

In the life of a female, adolescence is an important breakthrough. The female life does start from childhood, but there are certain milestones to reach a complete womanhood. A woman's life starts from completion of reproductive maturity which begins from puberty or the commencement of adolescence. One of the important aspects of the changes is the beginning of menstruation or menarche.

The start of menstruation and its continuation is based on five factors and their complex interactions. Any interruption or problem in these functions leads to amenorrhoea. The factors are (i) Normal female chromosomal pattern (ii) Anatomical patency of genital tract (iii) Normal HPO axis (iv) Responsive endometrium and (v) Active support from other endocrine glands e.g. Adrenal and Thyroid.<sup>14,15</sup>

First 2 -3 years after start of menarche are important because in these initial adolescence year's menstruation is usually not regular. But persistence of amenorrhoea could be due to any abnormality and can have substantial medical morbidity. Amenorrhoea has much implication on health like oestrogen deficient amenorrhoea can decrease bone mineral density which can cause fractures. Similarly amenorrhoea due to oestrogen excess can cause

dysfunctional uterine bleeding and increases risk of endometrial carcinoma. In both of these situations proper intervention is required to lessen the morbidity.<sup>16</sup>

In our study it was found that the mean age of the women in the study was  $19.46 \pm 3.54$  years with maximum patients of age between 16-20 years followed by 21-25 years. According to the results it was found that majority of the patients (66.07%) had height range of 126-150cm but a large number of patients 44% had height less than 125cm. which are supported by many other studies like in a study, Maliye et al<sup>17</sup> who found a mean height of 143 cm. Weight of main bulk (35.71%) of patients was found 46-50 kg. Only (7.14%) patients had weight more than 60 kg.

A detailed physical examination is required to identify the secondary sex characteristics. Normal breast development is an indicator for both normal ovarian production of oestrogens and peripheral conversion of androgen to oestrogen. Complete breast development occurs from peripheral conversion, therefore the presence of secondary sexual characteristics is really essential for assessing patients for investigation.<sup>18</sup>

In our study it was noticed that (37.50%) patients had infantile breast development and (62.35%) had well developed breast. The pubic and axillary hair development was infantile in (35.71%) and (30.36%) patients and they were well developed in (64.29%) and (69.64%) patients respectively.

Anatomical defects were found in 25 (44%) patients of primary amenorrhoea making it as the commonest cause. Some studies have found similar results that anatomical defects are the commonest, e.g. Khatoon H et al, found (69.5%)<sup>19</sup> patients as having

anatomical defects in their study sample but most of the studies found higher rate than this study like 60% and 69% in two different studies.<sup>5,20</sup>

Previous researches have elaborated that genetic factors like single gene disorders, chromosomal, or multifactorial disorders are also responsible of primary amenorrhoea. Among them chromosomal abnormalities are most common.<sup>21</sup> The proportion of chromosomal abnormalities varies from 15.9% to 63.3 % in primary amenorrhoea.<sup>22</sup>

Chromosomal defects in our study were also very common being found in (31%) patients, the cause was chromosomal defect, which is in accordance with the literature e.g. in a study, Rajangam found that 34.57% patients had chromosomal abnormalities.<sup>23,24</sup> Similarly in our study we found that HPO axis defects is also quite a common cause (18%) of primary amenorrhoea.

Different treatment modalities are available for regular menses and fertility potential but the outcome is not so satisfactory. Artificial reproduction is becoming a common practice with advancement of technologies which is a hope for some patients with primary amenorrhoea to have their genetic offspring(s). But these facilities are expensive and not easily available. In this situation, proper counseling of the patient and her relatives is very important.

## Conclusion

We demonstrated that main cause of the amenorrhoea in these patients was related to anatomical defects and was proven to be the most common cause of primary amenorrhoea. Chromosomal defects were the second and HPO axis defects were recorded as third leading cause of

amenorrhoea among patients suffering from primary amenorrhoea. In some patients some other defects (like TB endometritis) were also detected.

## References

1. Ray S, Sarkar RS, Mukhopadhyay P, Bisai S. Adolescent menstrual problem in a form of primary amenorrhoea-a challenge to gynaecologist. *AdvanBiol Res* 2011;5(5): 255-259.
2. Kwon SK, Chae HD, Lee KH, Kim SH, Kim CH, Kang BM. Causes of amenorrhoea in Korea: Experience of a single large center. *ClinExpReprod Med* 2014;41:29-32.
3. Marsh CA, Grimstad FW. Primary amenorrhoea: diagnosis and management. *ObstetGynecolSurv* 2014 ;69:603-162.
4. Maruthini D, Balen A. Modern management of amenorrhoea. *Trend UrolGynaecol Sex Health* 2008;13(2):24-28.
5. Khatoon H, Choudhury TA, Mahmud N. Primary amenorrhoea: analysis of 108 cases. *South Asian Fed Obstet Gynecol* 2010;2(2):105-108.
6. Ayatollahi H, Safaei A, Vasei M. Cytogenetic analysis of patients with primary amenorrhoea in southwest of Iran. *Iran J Pathol* 2010;5(3):121-126.
7. Pace G, Navarra F. The Mayer-Rokitansky-Kustner-Hausler syndrome..*Arch ItalUrolAndrol* 2007;79(1):39-40.
8. Gendall KA, Joyce PR, Carter FA, McIntosh VV, Jordan J, Bulik CM. The psychobiology and diagnostic significance of amenorrhoea in patients with anorexia nervosa. *Fertil Steril* 2006; 85(5):1531-1535.
9. Gabel KA. Special nutritional concerns for the female athlete.*Curr Sports Med Rep* 2006; 5(4):187-191.
10. Swenne I. Weight and growth requirements for menarche in teenage girls with eating disorders, weight loss and primary amenorrhoea. *Horm Res* 2008; 69(3):146-151.
11. Pinheiro AP, Thornton LM, Plotnicov KM. Patterns of menstrual disturbance in eating disorders. *Int J Eat Disord.* 2007; 40 (5):424-434.
12. Pradhan M, Manisha, Singh R, Dhingra S. Celiac disease as a rare cause of primary amenorrhoea:

- a case report. *J Reprod Med* 2007;52(5):453-455.
13. Rizwan N, Abbasi RM. Frequency of primary amenorrhoea and the outcome of treatment at Liaquat university hospital. *LiaquatUni Med Health Sci* 2008;7(2):110-114.
  14. Rokade, S. and A. Mane. A study of age at menarche, the secular trend and factors associated with it. *Internet J. Biological Anthropology* 2009;3:2.
  15. Maliye, C.H., P.R. Deshmuldi, S.S. Gupta, S. Kaur, A.M. Mehendale and B.S. Gag. Nutrient intake amongst rural adolescent girls of Wardha. *Indian J. Community Med* 2010;35(3):400-402.
  16. Golden NH, Carlson JL. The pathophysiology of amenorrhoea in the adolescent. *Ann N.Y. Acad. Sci* 2008;1135:163–178.
  17. Maliye, C.H., P.R. Deshmukh, S.S. Gupta, S. Kaur, A.M. Mehendale and B.S. Garg. Nutrient intake amongst rural adolescent girls of Wardha. *Indian J. Community Med* 2010; 35(3): 400-402.
  18. Ghazi A, Jabbar S. Frequency and causes of primary amenorrhoea at Civil Hospital Karachi. *Pak J Surg* 2004;20(1):35-37.
  19. Khatoon H, Chowdhury TA, Mahmud N. Primary amenorrhoea; analysis of 108 cases. *South Asian Fed Obstet Gynaecol* 2010;2(2):105-108.
  20. Laxmi KV, Babu SJ, Dayakar S, Mehrothra RN, Goud KI. Cytogenetic investigation of patients with primary amenorrhoea. *Indian J Hum Genet* 2012;18(1): 112–116.
  21. Rajangam S, Nanjappa L. Cytogenetic studies in amenorrhoea. *Saudi Medical Journal* 2007; 28(2):187-192.
  22. Dutta UR, Ponnala R, Pidugu VK, Dalal AB. Chromosomal abnormalities in amenorrhoea: A retrospective study and review of 637 patients in south India. *Arch Iran Med* 2013; 16(5):267-270.
  23. Rajangam S, Nanjappa L. Cytogenetic studies in amenorrhoea. *Saudi Med J* 2007;28(2):187-192.
  24. Samarakoon L, Sirisena ND, Wettasinghe KT, Kariyawasam KW, Jayasekara RW, Dissanayake VH. Prevalence of chromosomal abnormalities in Sri Lankan women with primary amenorrhoea. *J ObstetGynaecol Res* 2013;39(5):991-997.

---

“Every encounter is time bound with Swiss Precision.”

Siraj uddin Aziz