# **Original Article**

# FREQUENCY OF DISTURBANCE OF HORMONAL PROFILE (LH TO FSH RATIO) IN GIRLS OF AGE GROUP 14-18 YEARS WITH PRIMARY AMENORRHOEA

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## ABSTRACT INTRODUCTION

## **Objective:**

To determine the frequency of disturbance of hormonal profile (LH/FSH ratio) in girls of age group 14-18 years with primary amenorrhoea.

## Study Design:

Descriptive cross sectional study

#### Setting:

Outpatient departments of obstetrics and gynecology departments of University Medical and Dental College and Punjab Medical & Dental College Faisalabad.

#### Methods:

Ninty five patients who met the inclusion criteria were selected for study through obstetrics and gynaecology outpatient departments. Exclusion criteria was strictly followed to limit the confounding variables. After detailed history and examination, serum LH and FSH levels were performed in all patients. According to results of investigations, disturbance of hormonal profile(LH/FSH ratio) was determined.

### **Results:**

Out of 95 patients of age group 14-18 years with primary amenorrhoea, 6 (6.3%) were found to have disturbed LH to FSH ratio (Poly cystic ovarian Disease).

## **Conclusion:**

It is important for health care providers to recognize that poly cystic ovarian disease can be a cause of primary amenorrhea, so that appropriate investigation and management strategies may be undertaken. The results of this study support screening for polycystic ovarian disease in pre menarchal and adolescent girls in an effort to improve the reproductive health of these girls.

Key Words: Primary amenorrhoea, Polycystic ovarian disease, Disturbance of LH/FSH ratio

## INTRODUCTION

Primary amenorrhoea is defined as absence of menstruation by 14 years of age when there is no visible secondary sexual development or

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by 16 years of age in the presence of normal secondary sexual characteristics.

The menstrual cycle is regulated by complex interactions between the ovaries, pituitary and hypothalamus. A disruption at any point in any one of these pathways may lead to irregularities in the menstrual cycle and even amenorrhoea. In particular, amenorrhoea, the cessation of menstrual functioning, serves as an indicator of ovarian, pituitary and/or

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### hypothalamic dysfunction.(1)

Causes of primary amenorrhoea should be evaluated in the context of the presence or absence of secondary sexual characteristics which develop as a result of endocrine maturation at puberty and are development of breast, pubic and axillary hair, growth spurt and onset of menstruation.(2)

When secondary sex characteristics are normal, the underlying causes of primary amenorrhoea could be outflow tract obstruction, Turner syndrome, resistant ovary syndrome, polycystic ovarian syndrome, androgen insensitivity and constitutional delay. In the absence of secondary sex characteristics, primary amenorrhea could be due to hypothalamic pituitary dysfunction and ovarian failure. Heterosexual development could also lead to amenorrhoea.(3) Α thorough history and physical examination focusing on pubertal development assist in diagnosis and management.(4)

The association of primary amenorrhoea with polycystic ovarian disease has long been underestimated. Owing to the increased incidence of polycystic ovarian disease in Asian population ,the number of vouna adolescent girls are visiting gynaecological department outpatient for primary amenorrhoea at an increasing rate. The presence of primary amenorrhoea is of great concern to gynaecologists as this represents a confusing and difficult dilemma encompassing congenital malformations, genetic defects, metabolic derangements, selective anterior pituitary failure and occasionally malignant tumors.(5)By simply investigating PCOD(polycystic ovarian disease) as cause of primary amenorrhoea will not only relieve the stress of other non-modifiable causes of amenorrhea but also give hope that simple life modifications will improve the style symptomatology of the disease.

The increasing prevalence of Polycystic ovarian disease is alarming in adolescent girls that has not only led to menstrual irregularities ,features of hyperandrogenism (acne , hirsutism) but also psychological stress of primary amenorrhoea.(6)

While observing various etiologies of primary amenorrhoea, it was found that prevalence of polycystic ovaries is 5.26 %.(7)

The existing evidence evaluating PCOD as a cause of primary amenorrhoea is week. Very studies have been conducted to few determine the contribution of PCOD in primary amenorrhoea. This study helped to improve facilities to diagnose hormonal imbalance (disturbance of LH to FSH ratio) and expertise for developed its better management. The rationale of the study was to determine the frequency of disturbance of hormonal profile [LH to FSH ratio] that is indicative of PCOD in girls of age group 14 -18 years with primary amenorrhoea

## DATA COLLECTION PROCEDURE

The study was conducted in out patient departments of obstetrics and gynaecology at Madina Teaching hospital affiliated with University Medical and Dental college and Punjab Medical and dental college from Jan 2012 to Dec 2012. Patients who met the inclusion criteria (girls of age group 14-18 years with primary amenorrhoea) were selected for study through gynaecology and obstetrics outpatient departments. Primary amenorrhoea for the purpose of study was described as absent secondary sex characteristics by 14 years of age or presence of secondary sex characteristics but no menstruation by 16-18 years of age. Diagnostic clinical criteria was based on Tanner classification (table 1)

Exclusion criteria included iatrogenic primary amenorrhoea radiotherapy due to or chemotherapy in early childhood, outflow tract obstruction and absent uterus(diagnosed on pelvic ultrasonography). Detailed history and physical examination including secondary sexual characteristics, (pubic and axillary hair ,breast development) was performed. Pelvic ultrasonography was undertaken to evaluate the genital tract abnormalities and the presence or absence of uterus of patient. Ethical issues were addressed by explaining the patient risks( costly investigations) and benefits that is improvement of reproductive health and psychological and menstrual benefits by confirmation of a treatable cause of primary amenorrhoea. The study was approved by institutional research ethical review committee.

Initial evaluation of the patients was done by taking detailed history including age, height, and family history of genetic weight, abnormalities, nutritional and dietary factors, systemic diseases, previous surgeries, prior diagnostic studies and results. Patients and family members were reassured regarding the confidentiality of the data obtained from them. After proper informed consent these patients were thoroughly examined. General physical examination was done to note the appearance, height, weight and secondary sex characteristics (breast, pubic and axillary hair development), based on Tanner classification.(table 1) Abdominal examination was performed to see any lower abdominal mass. Limited pelvic examination was done to see the external genitalia. History and examination were done by the researcher herself.

In all these patients serum levels of follicle stimulating hormone [FSH] and luteinizing hormone [LH] were done by the pathologist of PINUM [Punjab institute of nuclear medicine] cancer hospital .According to results of investigations, disturbance of hormonal profile [LH to FSH ratio] was determined. Normal value was taken as 1 IU/L .A value > 1 IU/L was labeled as disturbed ratio.

SPSS version 10.0 was used for data analysis.

Descriptive statistics included mean <u>+</u> Standard Deviation of continuous data that is Age, Height and Weight of the patients. Frequency [percentages] was calculated for categorical data that is ;disturbance of hormonal profile[LH/FSH] and were presented in form of tables and graphs.

### RESULTS

Age group of patients included in this study was 14-18 years with mean age of 16 years.(Table 2). Minimum height of the patients was 5 feet and maximum was 5 feet 6 inches with mean of 5.2632feet (Table 2) Weight of the patients was in range of 50-70 kgs with a mean of 54 kgs.(Table 2)

Secondary sex characteristics were present in 95 patients (100%).(Table 3) Hormonal profile was done in all patients and it included serum LH, FSH and LH/FSH ratio. Mean value of serum FSH was 8.0000 U/L and the range was 6.00 to 10.00 U/L. Mean value of serum LH was 8.2737 U/L with the range of 6.00 to 16.00 U/L. LH/FSH ratio ranged from 1.00 to 1.70 with the mean of 1.0316 U/L. (Table 4) Hormonal profile (LH/FSH ratio) was disturbed in 6 patients (6.3%) out of 95 and was found normal in 89 patients (93.7%) out of 95. (Table 5)

Stage	Breast development	Pubic hair
1	Refers to prepubertal state and includes no palpable breast tissue, with the areolae less than 2cm in diameter. The nipples may be inverted, flat or raised.	There are no sexually stimulated pubic hair present, but some nonsexual hair may be present in the genital area.
2	Breast budding occurs, with a visible and palpable mound of breast tissue. The areolae begin to enlarge, the skin of areolae thins, and the nipple develops to varying degrees	Is characterized by the first appearance of coarse, long, crinkly pubic hair along the labia majora.
3	Is reflected by further growth and elevation of the entire breast. When the individual is seated and viewed from the side, the nipple is generally at or above the mid plane of breast tissue.	Coarse, curly hair extend onto the mons pubis

Table No	<b>5 1</b> .	Tanner	classification
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4	In most girls, it is defined by projection of the areola papilla above the general breast contour in a secondary mound.	is characterized by adult hair in thickness and texture, but the hair are not distributed as widely as in adults and typically do not extend onto the inner aspects of thighs.
5	Breast is mature in contour and proportion. In most women ,the nipple is more pigmented at this stage than earlier in development, and Montgomery's glands are visible around the circumference of the areola. The nipple is generally below the mid plane of breast tissue when the woman is seated and viewed from the side.	Pubic hair extend onto thighs

## Table No: 2

### Age, Height and Weight distribution (years, feet, kgs respectively)

Parameters	Ν	Minimum	Maximum	Mean	Std. Deviation
Age of the patients	95	14	18	16.02	1.26
Height of patients	95	5.00	5.60	5.2632	.1297
Weight of patients	95	50	70	54.24	3.28

## Table No: 3

#### Secondary sexual characteristics

Secondary sexual characteristics	Frequency	Percentage	
Present	95	100	

#### Table No: 4

#### Hormonal profile (Units/Litre)

Hormones	N	Minimum	Maximum	Mean	Std.Deviation
Serum FSH	95	6.00	10.00	8.0000	1.2291
Serum LH	95	6.00	16.00	8.2737	1.7470
LH/FSH ratio	95	1.00	1.70	1.0316	.1265

#### Table No: 5

### Disturbance of hormonal profile (LH/FSH ratio)

Disturbance of hormonal profile(LH/FSH ratio)	Frequency	Percentage
Yes	6	6.3
No	89	93.7
Total	95	100.0
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### DISCUSSION

Primary amenorrhoea creates problems such as social, psychosexual, infertility, osteoporosis and genital atrophy. Whenever a child presents with her parents and concern is expressed about her wellbeing, it is important to record history and examination and then to institute appropriate diagnostic investigations. However, a thorough physical examination is extremely important to identify the presence or absence of secondary sex characteristics.(7)

Polycystic ovarian disease (PCOD) is a complex, multifaceted, heterogeneous disorder. It is one of the most common causes

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of anovulation and amenorrhoea. However, heterogeneous clinical features of the polycystic ovarian disease may change throughout the lifespan, starting from adolescence to postmenopausal age group, largely influenced by obesity and metabolic alterations, the phenotype of women with polycystic ovarian disease is variable, depending upon the ethnic background.(8)

Irrespective of the geographic locations, a rapidly increasing prevalence of polycystic ovarian disease(PCOD) has been reported in Asian Indians , suggesting that primary prevention strategies should be initiated early in this ethnic group.(8)

Prevalence is also rising in adolescent girls and they are even presenting with primary amenorrhoea which is a rare association. Because of this increase in the magnitude of polycystic ovarian disease and its association with primary amenorrhoea studies are being conducted all over the world.(8)

This study was conducted at Madina teaching hospital and Allied hospital, Faisalabad serving a population of about 5-6 millions . The patients coming through outpatient departments were enrolled in study. Total patients included in study were 95 which presented with primary amenorrhoea and were of age group 14-18 years. Out of 95 patients, 6 (6.3%) were having disturbed LH/FSH ratio(PCOD) and the results of the study are similar to the study done in Liaquat University Hospital by Naushaba Rizwan and Razia Mustafa Abbasi in August 2008 but age group of their study was 10-30 years.(7)

In one study conducted in Paediatric and Adolescent gynaecology clinic, Hong Kong, by PW Chung in 2011, polycystic ovarian disease(PCOD) was found in 7% of primary amenorrhoeic patients(9)which is almost similar to our study (6.3%).This study was conducted on adolescents aged 14-19 years almost the same age group as in this study.

In another study conducted by Nduwayo L on primary amenorrhoea revealing micro polycystic ovary syndrome showed raised LH/FSH ratio in 6 out of 9(66.6%)

patients.(10) They studied association of PCOS and primary amenorrhoea clinically, Biochemically and ultrasonographically, whereas only biochemistry has been studied in this study.

One study was conducted by Van der Heyden JC, Janssens LP, Drop S in 2006 in which they studied hormonal disturbance in primary amenorrhoea.(11)This study showed raised values of both LH and FSH in 1 out of 2 (50%) patients with primary amenorrhoea, whereas in this study LH is raised more than FSH and so LH/FSH ratio is disturbed showing polycystic ovarian syndrome( PCOS).This girl with raised FSH and LH values was 18 years old showing similar age distribution.

The study held in March 2007 by Dr. Peter E Hughesdon in department of morbid anatomy, at University College Hospital Medical School, London on ovarian pathology in primary amenorrhoea, polycystic ovarian syndrome(PCOS) was found in 2 out of 16 (12%) patients, however in this study biochemistry has been studied instead of ovarian pathology.(12)

The study conducted in Division of Yoga and life sciences , SVYASA university, Bangalore ,India by Nidhi R in August 2011 showed that 29 (6.3%)girls of age group 15-18 years presented with oligomenorrhoea and polycystic ovarian syndrome ,while in this study primary amenorrhoea was associated with polycystic ovarian syndrome in the same age group.(13)

Marianna Rachmiel also found primary amenorrhoea as a manifestation of polycystic ovarian syndrome in adolescents of age group 14-18 years in their study.(14)

Although the link between Primary amenorrhoea and PCOD has been mentioned briefly in the literature, PCOD is rarely listed as a differential diagnosis for primary amenorrhoea. Although PCOD is becoming more prevalent in parallel with rising obesity rates, studies have not evaluated the clinical features of this subgroup of patients with primary amenorrhoea and PCO. Further

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studies to determine the frequency of this subgroup of patients are warranted.(15) **CONCLUSION** 

is an extremely Primary amenorrhoea stressful problem for a young girl and her parents. It is important for health care providers to recognize that primary amenorrhoea may be due to PCOD so that appropriate investigative and management strategies may be undertaken. The results of this study support screening for polycystic ovarian disease in pre menarchal and adolescent girls in an effort to improve the reproductive health of these girls.

The clinician should handle the cases with great sensitivity. Counsceling is of great importance in the management of cases of primary amenorrhoea.

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