

Prevalence of Elevated Luteinizing Hormone (LH)/Follicle Stimulating Hormone (FSH) Ratio in Polycystic Ovary Syndrome (PCOS) Women Among Local Population

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ABSTRACT

Objective: To assess the frequency of elevated LH/FSH ratio >1 in women with polycystic ovary syndrome among local population.

Study Design: Cross-sectional study.

Methodology: This cross sectional study was carried out at two tertiary care hospitals in Karachi during October 2010 to Feb 2011. A total of 163 PCOS women of reproductive age (18-40years) fulfilling revised Rotterdam 2003 criteria were studied. The data recorded on a prescribed proforma include current age, age at menarche, menstrual irregularities, presence of hirsutism, acne, infertility, familial nature, blood pressure, BMI, waist to hip ratio. Blood sample for gonadotropin assay were taken in random state on specific dates of menstrual cycle (day 6th to day 30th) in gel tube. Hormonal assay were performed using chemiluminescent immunoassay.

Results: Mean age of presentation of PCOS subjects was 24.88±5.35 years. Menstrual irregularities (99%) were the commonest presentation followed by acne (88%), hirsutism (71%) and infertility (62%). A high frequency (>71%) of elevated LH/FSH > 1 ratio was observed among local population.

Conclusion: The present study concludes that elevated LH/FSH ratio >1 is a characteristic finding of Pakistani population of PCOS (present in = 71% of patients) and with proper sampling dates can be used as diagnostic tool for establishing the diagnosis of PCOS.

Key words: PCOS; gonadotropin; BMI.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinopathy of childbearing bearing age women with an estimated prevalence of 4-12 %.¹⁻³ It is one of the leading causes of infertility in females.⁴ The features of PCOS are heterogeneous and vary with age ranging from premature puberty in childhood, menstrual cycle disturbances, obesity, acne, hirsutism and infertility in early adulthood and middle life to type II diabetes, cardiovascular diseases and malignancies later in life. However, usually patients present with classical description of menstrual irregularities, hyperandrogenism, central obesity and typical ultrasonographic findings around the time of menarche.⁵⁻⁶

In recent years health care professionals have begun to consider PCOS as a life time disorder with significant long term health risks.⁷ These risks includes insulin resistance, type II diabetes, dyslipidemia, cardiovascular diseases and even malignancies like cancer of endometrium.⁸⁻⁹

Furthermore the typical phenotypic expression of the disease makes PCOS women particularly in adolescent age group more vulnerable to emotional stress.¹⁰

Therefore, it seems very important to have an early and accurate diagnosis of the disease since early diagnosis and intervention can prevent or at least delay many of these maladies later in life. Even in most developed countries like USA the PCOS and its related complications are a huge economic burden (approximately \$4.37 billion annually).¹¹ Pakistan being a poor country with limited resources cannot bear such great losses.

Elevated LH/FSH ratio is typically seen in PCOS patients¹² and was also considered as a gold standard for clinical diagnosis of the disease during early 90's¹³ however became controversial by a number of studies which reported a variable prevalence (30-90%) among PCOS women.¹⁴⁻¹⁶ Even Rotterdam 2003 diagnostic criteria for PCOS, presently the most acceptable one, do not include it.¹⁷ All such studies were done on blood

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samples taken during the "early follicular phase" (Day 1-3) of menstrual cycle, when serum LH is normally suppressed and therefore may lead to under estimation of elevated LH/FSH ratio.

PATIENTS AND METHODS

This cross-sectional study was carried out at IBMS, DUHS Karachi in collaboration with Gynae/infertility clinics of two tertiary care hospitals in Karachi; Civil Hospital and Lady Dufferin Hospital. The research proposal was approved from Ethical Review Board of Dow University of Health Sciences and all subjects were enrolled voluntarily in the study after being explained by concerned doctor and signing the consent form. A total of 163 PCOS women of childbearing age (18-40years) fulfilling revised Rotterdam 2003 criteria were studied during the period from October 2010 to February 2011.

PCOS women who were pregnant, or on any contraceptive pills or oral hypoglycemic agents were excluded from the study. Also amenorrhic PCOS women were excluded from the study. A detail history was taken on a pre-structured proforma which includes current age, age at menarche, history of menstrual irregularity, acne, hirsutism, infertility, obstetric history, occurrence of similar cases in family. Complete physical examination including height, weight, body mass index (BMI) and Waist to Hip ratio, blood pressure was also recorded. For assessing the level of obesity, we used new Asian BMI classification.

For estimation of serum LH and FSH blood samples (5ml) were drawn in follicular phase of menstrual cycle (from 6th day of menstruation till 30th day) by venepuncture in random state. Whole blood was collected in SST gel clot activator tube. Serum was separated after a standardized time and subjected to chemiluminescent immunoassay for gonadotropin (LH/FSH). Statistical analysis were performed using the Statistical Package for the Social Sciences version 16.

RESULTS

Table-1 describe the demographic, clinical and hormonal characteristics of Pakistani population PCOS. Menstrual irregularities were the commonest presentation (99%) followed by acne (88.8%) Hirsutism (71.9%), and infertility (62.5%). Frequency of obesity in our studied population was 69%.

DISCUSSION

Polycystic ovary syndrome is a disease of public health importance as it is related with a number of long term significant health risks. The exact prevalence of PCOS in Pakistan is not known but in the neighboring countries

like Sri-Lanka and India the burden of disease is as high as 6.3% and 9% respectively.¹⁸⁻¹⁹ So a comprehensive approach to the evaluation and treatment of affected women is required.²⁰

This study was an attempt to explore the role of LH/FSH ratio as an indicator for PCOS at an early stage of investigation. This will be beneficial to both patients as well as physician for the better management of disease. LH/FSH ratio is a ratio between two gonadotropin hormones; LH and FSH. These two hormones are secreted by the β -cells of the anterior pituitary under the influence of the hypothalamic GnRH. In females, LH act on the theca cells of the ovary to cause androgen production from cholesterol, while FSH regulates function of granulosa cells that causes the conversion of the cholly derived androgens to estrogens by aromatase enzyme.²¹ A delicate balance of LH and FSH is required for early follicular development. In normal females LH/FSH ratio in early follicular phase is normally 1. If LH levels are too high, theca cells produced large amount of androgens causing follicular atresia. Both the absolute level of circulating LH as well as its ratio to FSH is significantly elevated in PCOS women.²² The increase in intraovarian androgens believed to play a significant role in anovulatory process. When any anovulatory state exists for a period of time affected women developed bilaterally enlarged polycystic ovaries—a hall mark of PCOS patient and a finding present in more than 80% of PCOS.

Abnormal gonadotropin secretion has been implicated in pathogenesis of PCOS and is very typical finding among such patients. However their role in identification of PCOS remains controversial. The international data showed a variable prevalence of 30-90% among PCOS women. In the recent years more stress has been paid to the day of menstrual cycle chosen for gonadotropin sampling as one of the possible reason for under estimation of elevated LH/FSH ratio and hence its controversial role in identification of PCOS. This seems quite logical as it is well recognized in literature that serum LH level is strongly correlated with days from natural or induced menses. Both exogenous progesterone (commonly prescribed to PCOS women for induction of withdrawal bleeding) and endogenous progesterone (associated with spontaneous ovulation) decreases serum LH secretion.^{12,23} This suppressive effect of progesterone is sustained even in early phase of next menstrual cycle.²³ Routinely measurement of serum LH and LH/FSH ratio are being done in early follicular phase of menstrual cycle i.e. day 1-3,¹⁷ when it is normally suppressed and therefore prevalence of elevated LH/FSH ratio is under estimated. and hence produce limited role in diagnosis of PCOS.

In the present study blood samples for gonadotropin were taken on specific days of menstrual cycle (from day 6th to day 30th) and the study results showed a high

Table 1: Descriptive Statistics of Study variables (n=163)

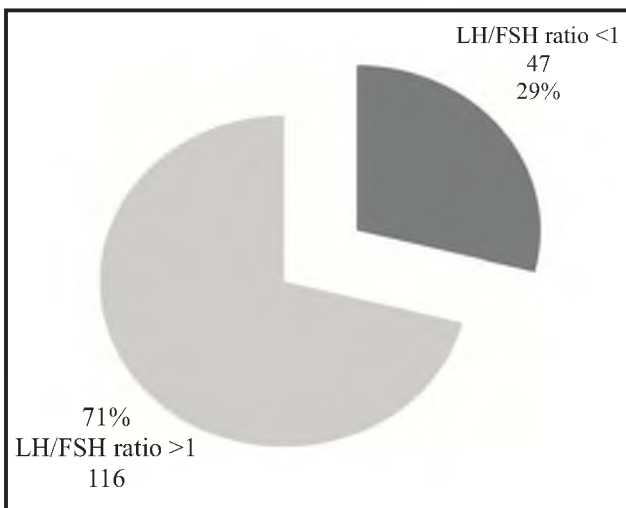
Demographic profile	n	Mean ± SD	Minimum	Maximum
Age (years)	163	24.88 ± 5.35	18	40
Height (m)	163	1.56 ± 0.05	1.4	1.7
Weight (Kg)	163	66.14 ± 11.02	48	121
BMI(Kg/m ²)	163	27.03 ± 4.42	20.2	44.44
Hip circumference(cms)	163	107.10 ± 9.16	86	139
Waist circumference (cms)	163	96.15 ± 10.58	72	124
Waist-hip ratio	163	0.89 ± 0.05	0.75	0.98
Clinical profile				
Systolic blood pressure(mmHg)	163	106.93 ± 8.91	90	130
Diastolic Blood Pressure (mmHg)	163	67.98 ± 7.64	60	90
Hormonal profile				
Serum LH(mIU/ml)	163	9.39 ± 7.08	1.15	54.2
Serum FSH(mIU/ml)	163	5.96 ± 2.84	1.51	18.5
LH-FSH ratio	163	1.72 ± 1.15	0.24	6.14

Table 2: Body Mass Index (Kg/m2) of PCOS patients (n=163)

BMI	No. of patients	%
Normal (18.5-22.9)	18	11.3
Overweight (23-24.9)	32	19.4
Obese I (25-29.9)	91	55.6
Obese II (= 30)	22	13.8

LH/FSH RATIO IN WOMEN WITH POLYCYSTIC OVARY SYNDROME n=163

A high prevalence of elevated LH/FSH>1 ratio was observed in present studied population of PCOS



frequency (71%) of elevated LH/FSH ratio >1 among Pakistani population of PCOS. This high frequency of elevated LH/FSH ratio is quite significant as it points towards its potential role in diagnosis of PCOS.

This study results are consistent with finding of Iwasa et al. in which they evaluated LH/FSH ratio in both in early and late follicular phase of PCOS women and found that in late follicular phase the prevalence of elevated LH/FSH ratio was much high (89%) as compare to early follicular phase when it is only elevated in 52% of patients only. Therefore they also recommended late follicular sampling.²³

These results are also consistent with findings of Hsu et al. (2009) in which they evaluated 251 PCOS women in specific days of menstrual cycle and found that 70% of such women have elevated LH/FSH ratio >1. Therefore they also concluded that the LH-FSH ratio is a valuable diagnostic tool in evaluating women with PCOS and an LH-FSH ratio of >1 may be used as a decision threshold.²⁴

These results are also in accordance with the findings of Hendrick et al. who did a study on PCOS women and also concluded gonadotropin assays should not be done during early follicular phase (day 1-5) as it is normally suppressed during this phase.²⁵

LH/FSH ratio seems to be a better choice to be assessed as an indicator of disease in comparison with other two parameters ultrasound and serum testosterone. Currently transvaginal u/s is considered to be the gold standard for PCOS diagnosis²⁶ but this is not suitable for unmarried girls especially in our culture.

As far as serum testosterone levels are concerned a number of physiological factors influences serum testosterone level like its pulsatile release during the day,²⁷ diurnal rhythm (am > pm)²⁸, its relation with phases of menstrual cycle (luteal > follicular)²⁹ and age in years (20 s >40 s).³⁰

CONCLUSION

The present study concludes that elevated LH/FSH ratio >1 is a characteristic finding of Pakistani population of PCOS (present in = 71% of patients) and with proper sampling dates can be used as diagnostic tool for establishing the diagnosis of PCOS.

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