Polycystic ovarian syndrome: the correlation between the LH/FSH ratio and disease manifestations

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ABSTRACT

Objectives: to study the correlation and association among LH / FSH ratio, BMI and clinical manifestations of Polycystic Ovarian Syndrome (PCOS).
Setting: Institution of Infertility Treatment and Embryo Research.
Study design: A cross sectional descriptive study.
Materials and Methods: One hundred and seven infertile women with PCOS were included according to their menstrual history (Amenorrhea or oligomenorrhea) and/or presence of hirsutism. All of them were subjected to vaginal ultrasound to confirm the presence of polycystic ovary. Body Mass Index (BMI) assessed to be included in the correlations. Blood collected twice (4-5 days interval) from each attendant to measure their serum FSH, LH & mean LH/FSH ratio obtained. The resulted data were arranged in tables and subjected for statistical study using correlation analysis.
Results: The characteristics of women recruited, showed that 59.81% of them were 25-32 years old, and 63.55% of them were over weight or obese (BMI>25). Besides the infertility, the commonest second complaint was hirsutism (64.49%) While oligomenorrhea is prevalent in 43.93%, amenorrhea in 22% and only minority (6.56%) have regular menses. The relationship between study variables as assessed by correlation analysis revealed no statistical significant correlation among LH/FSH ratio, BMI and other manifestations (hirsutism and oligomenorrhea).
Conclusion: No significant statistical correlation is found between LH/FSH ratio, BMI, menstrual pattern and hirsutism. This disproves the traditional concept about PCOS which regards that the heavier the patient is the higher the LH or the worst manifestations.
Key words: PCOS, BMI, Hirsutism

Polycystic Ovarian Syndrome (PCOS) is probably the most prevalent endocrinological disorder affecting women and it is the most common cause of menstrual disturbance during reproductive age. It characterizes by presence of

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polycystic ovaries on ultrasound together with the clinical & biochemical signs of hyperandrogenism (1).

Adams et al (2) described that, PCOS has no constant manifestation apart from the criteria seen by vaginal ultrasound (10 or more cysts, 2-8 mm in diameter, arranged around an echo-dense stroma) which appears to be the most sensitive diagnostic marker for PCOS . Furthermore, Takahashi et al (3) reported that, an ovarian volume > 6.2ml and follicles> 10 with a diameter

of 2-8 mm are the Transvaginal Ultrasound criteria of PCOS seen in 94 % of those women.

On the other hand, Dunaif A et al (4) claimed that, polycystic morphology is consistent with, but not essential for, the diagnosis of the syndrome. These changes, however, can be present in women who are endocrinologically normal. Thus, the ovarian morphological change must be distinguished from the endocrine syndrome of hyperandrogenism and anovulation (5, 6).

The current diagnostic criteria for PCOS defined during a consensus symposium held in Rotterdam, in May 2003, sponsored by the European Society of Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM). Diagnosis depends on two of the following criteria only: Clinical and/or biochemical evidence of hyperandrogenism, with exclusion of other causes of androgen excess; Oligo or anovulation and Polycystic ovaries.

Moreover, manifestations of PCOS may include menstrual irregularities, obesity, insulin resistance and elevated serum LH levels (7).

The characteristic increase in LH relative to FSH release, have long been appreciated in PCOS. Because of the pulsatile nature of their release, a single test fails to detect an increased LH/FSH ratio. This, as well as its lack of specificity, has led to the recommendation that LH/FSH ratios not be included in the diagnostic criteria for PCOS (4, 8).

Approximately half of PCOS women are obese or overweight and obesity has important role in the development of the Hyperandrogenic State (9, 10). Even those with normal BMI, PCOS sufferers tend to have android body type with waist –to-hip ratio greater than 0.8 (11).

Both obese and nonobese PCOS women are insulin resistant and hyperinsulinemic with positive correlation between degree of hyperandrogenism and that of the hyperinsulinism (9,12), however, higher levels of androgens and more pronounced insulin resistant were demonstrated in obese PCOS women compared with leaned PCOS patients (13).

In this study we aimed to find a correlation or association among LH/FSH ratio, BMI, and Hirsutism and menstrual patterns in women suffering from PCOS.

MATERIAL AND METHODS

In this study, 107 women in their reproductive age suffering from infertility had been included in a cross sectional descriptive study conducted at the Institution of Infertility Treatment and Embryo Research. They attended the Institution seeking for therapy for their infertility. They were selected and diagnosed to have PCOS on the bases of their menstrual history (Amenorrhea for more than 6 months or oligomenorrhea <6 menstrual periods/year) and /or having hirsutism defined by Ferriman-Gallwey score > 8 and presence of polycystic ovary.

All women included had polycystic ovary as judged by vaginal ultrasound (6.5 MHZ probe), finding more than 10 follicles of a diameter between 2 and 8 mm with an ovarian volume exceeding 6.2 ml was taken to be diagnostic.

Body mass index (BMI) was measured, for each, using the formula; wt (kg)/ht (m^2) and the measurements were scored to classify their state of obesity.

Two blood samples were taken, first at cycle day 4-6 from those with regular cycles or at any day from those with amenorrhea or those with completely irregular cycles and a second sample obtained 3-4 days later according to the patient availability to measure their serum FSH & LH levels using Radioimmunoassay technique, then mean LH/FSH ratio obtained.

The data were arranged in tables and subjected for statistical study using correlation analysis and chi- square test (χ^2- test).

Statistical analysis

The analysis was carried out using SPSS version 12. After computing descriptive statistics, the data were subjected for correlation analysis by correlation coefficient (Pearson correlation) which represented by the letter (r) and indicates the degree of relationship between the variables. r values lie between -1 and +1, If r = +1 there is a perfect linear correlation, while r = -1 indicates a perfect inverse linear correlation. If r= 0 the two variables are not correlated (14).

Table 1. Characteristic of the sample distributed by Age, BMI, Hirsutism and Menses

Age	No.	Percentage
17-24	30	28.03%
25-32	64	59.81%
33-36	9	8.41%
37-44	4	3.73%
Total	107	100%
BMI	No.	Percentage
18-25	39	36.45%
25.1-30	36	33.64%
30.1-35	24	22.43%
>35	8	7.48%
Total	107	100%
Hirsutism	No.	Percentage
Positive	69	64.49
Negative	38	35.51
Total	107	100%
Menses	No.	Percentage
Oligomenorrhea	47	43.93%
Irregular	29	27.10%
Amenorrhea	24	22.40%
Regular	7	6.54%
Total	107	100%

To confirm further association to inferential statistic, χ^2 test was applied for categorical variable and p value <0.05 considered to be significant.

RESULTS

The characteristics of women included in this study concerning their Age, BMI, hirsutism and menstrual status are shown in table 1.

The majority of our sample (59.81%) were 25-32 years old and only 36.45% of them were regarded within normal BMI (≤25).

Two third of the participants (64.49%) suffer from of hirsutism. Moreover, the study shows that nearly half of the women included complain of oligomenorrhea (43.93%) and about fifth of them suffer from Amenorrhea (22.40%), while those with regular menses are minority (6.45%).

Figure 1, shows that two-third of study sample (64 %) have high mean LH/FSH ratio (more than 2), while only (36%) of them with a ratio equal or less than 2.

Correlation among LH/FSH ratio, BMI, Hirsutism and Menses

The relationship between the study variables was assessed by correlation analysis, table (2).

Regarding LH/FSH ratio and BMI there was no significant statistical correlation found (r=0.014, P>0.05), moreover, there was no evidence of specific association. Similarly, there were no significant correlations between LH /FSH ratio and Hirsutism (r=0.06, P >0.05) and between LH/FSH and menstrual pattern (r= -0.08, P > 0.05).

LH/FSH ratio and other PCOS manifestations

Inferential Statistical χ^2–test was applied among the variables (LH/FSH ratio from one side and age of the patients, BMI, state of Hirsutism and menstrual status from another side). No statistical significant associations (P > 0.05) were found, table (3).

Furthermore, there is no statistically significant association found between BMI and Menstrual pattern, χ^2= 2.9 (P= 0.35) and between BMI and Hirsutism, χ^2=1.4 (P= 0.22).

DISCUSSION

Although PCOS is a relatively common disorder with a 5–10% prevalence among women of reproductive age, its etiology remains unknown (8).

It is emphasized that, PCOS is a syndrome with no significantly single diagnostic criterion (such as hyperandrogenism or polycystic ovaries) is sufficient for clinical diagnosis (7).
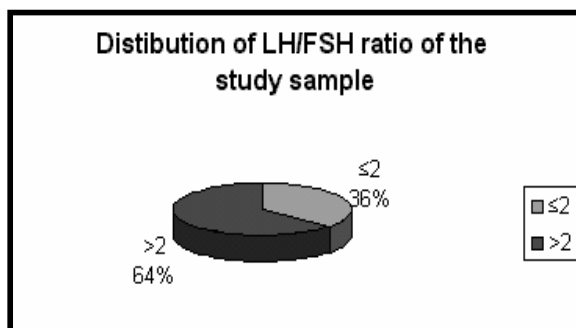

Figure 1. Distribution of mean LH/FSH ratio of the study sample

Table 2. Pearson's Correlation among LH/FSH ratio, BMI, Hirsutism, Menses

Pearson Correlation	LH/FSH	BMI	Hirsutism	Menses
LH/FSH	1.000	0.014	0.066	0.083
BMI	0.014	1.000	0.096	0.014
Hirsutism	0.066	0.096	1.000	0.172
Menses	0.083	0.014	0.172	1.000

The clinical consequence of chronic anovulation is some form of menstrual irregularity ranging from oligomenorrhea (menses every 6 weeks to 6 months), amenorrhea or dysfunctional uterine bleeding. Infertility may be the presenting symptom of the anovulation (5, 15).

In this study the basic finding upon which diagnosis of PCOS was made is the presence of polycystic ovary by vaginal ultrasound which was done to all participants by same physician plus the suggestive clinical findings "amenorrhea or oligomenorrhea and /or hirsutism", fulfilling the Rotterdam updated criteria of PCOS (7).

Out of the 107 women included in the study, 29 of them had completely irregular menses (complete loss of cycle pattern and bleeding always unexpected) and 6 of them still have regular menses in spite of evident hirsutism.

PCOS is reported to be more prevalent in younger ages (<35) than among older women, proposing that due to a physiological decline of the follicular cohort leading to a normalized ovarian ultrasonographic appearance with advancing age (16), this is in consistence with our notice when finding that 87.84% of the patients included in the study were less than 32 years of age.

Regarding the BMI, 63.55% of the participants were overweighed (BMI> 25kg/m2) this result is higher than what is reported by Pasquali et al (9) and Kiddy et al (17), who found that about 50% and 35% of the women with PCOS are obese or overweight respectively. The explanation for our higher incidence of overweight may be attributed to the food habits adopted in Iraq and to the lack of exercise among Iraqi women.

Table 3. Distribution of the mean LH/FSH ratio by the Age, BMI, Hirsutism, and Menstrual pattern

Mean LH/FSH ratio		≤2	>2	Total
Variable				
Age	≤30	29	55	84
(1*)	>30	10	13	23
Total		39	68	107
BMI	18-25	14	25	39
(2*)	>25	25	43	68
Total		39	68	107
Hirsutism	+ve	22	47	69
(3*)	-ve	17	21	38
Total		39	68	107
Menstrual pattern	Oligomenorrhea	15	32	47
(4*)	Amenorrhea	9	15	24
	Irregular menses	13	16	29
	Regular menses	2	5	7
Total		39	68	107

1* $\chi^2 = 0.53$ df=1   p= 0.40
2* $\chi^2 = 0.13$ df=1   p= 0.93
3* $\chi^2 = 2.5$ df=1   p= 0.19
4* $\chi^2 = 2.1$ df=3   p= 0.60

Hirsutism was the second common complaint to infertility that the attendants claimed to suffer; it is prevalent in 64.49% of them. This result is relatively close to the figure 73% obtained by Kiddy et al (17). Besides to what the patient told us about her concern and suffer from abnormally excessive hair growth she got, deciding the state of hirsutism was only made after seeing the reality of excessive and coarse hair covering unusual areas of here body like chin, chest, abdomen and legs. Hirsutism was regarded positive when Ferriman-Gallwey scoring exceeds 8.

Abnormality of the hypothalamic-pituitary-ovarian or adrenal axis has been implicated in PCOS. Disturbance in the pulsatility of gonadotrophin releasing hormone (GnRH) results in the relative increase in LH to FSH release (10). An abnormal feedback mechanism by ovarian estrogen is blamed to play role in this discriminated increase in LH release (18). As a result of this derangement the ratio between FSH and LH levels which is normally around 2 to 1, become reversed and sometimes even more (2 or 3 to 1) in approximately 60% of the patients with PCOS (19), which agree with the results obtained in this study where about 2/3rd of the women with PCOS have high LH/FSH ratio (LH/FSH ratio >2 is 64%), (Figure 1).

Banaszewska et al (20), regarded abnormal LH/FSH ratio when it is greater than 2 and 4.5.4% of PCOS women having an elevated ratio, furthermore they found that most of PCOS women with normal ratio suffer from hyperinsulinemia and obesity while those with hyperinsulinemia and excess LH constitute a distinct subgroup with increased adrenal androgenic activity.

On the other hand, Cho LW et al (21) found that, LH/FSH ratio has little use in diagnosing polycystic ovarian syndrome because the median LH/FSH ratio did not differ significantly between the PCOS and non affected group.

The traditional belief that obesity plays a serious role in the pathophysiology of PCOS dated back to years of Stien Leventhal but the puzzling fact that not all PCOS women are obese, moreover, not every women with PCOS has an abnormal LH/FSH ratio nor they all posses the hormonal and biochemical changes suggested to the disease. This diversity in disease criteria inspired us to think

about measuring correlations between disease manifestations and to answer the question "does higher BMI necessarily indicate a higher LH/FSH ratio or greater incidence of hirsutism or menstrual disturbance."

Some studies admit that there are some correlations for example, Insler et al (22), reported that, the none obese PCOS women had significantly higher level of serum LH than obese counterparts and Yanira et al (23) agreed that an inverse relationship between LH and BMI in PCOS, their study suggests that the effect of BMI on LH is mediated at pituitary level and not a hypothalamic level in those patients.

Kiddy et al (17) found an inverse correlation of FSH with BMI in obese PCOS and there is increased frequency of hirsutism in obese compared with lean PCOS women.

When we tried to find correlations between mean LH/FSH ratio and PCOS manifestations (BMI, menstrual patterns and hirsutism). No significant statistical correlation was found as shown clearly in table 3 and moreover, no statistically significant association obtained between each variable with the other (P value >0.05).

Our results may provide an answer to the question raised before disproving the traditional concept of the disease which regards that the heavier the patient is the higher the LH or the worst disease manifestation, in my view this may add more to the disease mystery.

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