ORIGINAL ARTICLE

# LUTEINIZING HORMONE TO FOLLICLE STIMULATING HORMONE RATIO IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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**Background:** Polycystic ovary syndrome is the most commonly occurring endocrinopathy in females of reproductive age group. It is characterized by a wide range of signs and symptoms resulting from hormonal derangements leading to reduced fertility. **Methods:** This was a cross-sectional (comparative) study. We took 40 cases of polycystic ovary syndrome and 40 controls of infertility without polycystic ovary syndrome depending on the presence of clinical features and ultrasound scans. Blood samples were collected and assayed for luteinizing hormone and follicle stimulating hormone. Data was analyzed with SPSS-19. **Results:** Luteinizing hormone to follicle stimulating hormone ratio was raised in 3 out of 35 patients (8%) in cases and in 2 out of 39 patients (5%) in controls. There was no statistically significant difference in the luteinizing hormone levels and the follicle stimulating hormone levels and the luteinizing hormone to follicle stimulating hormone ratio of the two groups as indicated by a *p*-value> 0.05. **Conclusion:** Luteinizing hormone to follicle stimulating hormone ratio was not found to be raised in majority of the polycystic ovary syndrome patients included in this study.

**Keywords:** Polycystic Ovary Syndrome; Luteinizing Hormone; Follicle Stimulating Hormone; Infertility

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age group which affects 6–10% of premenopausal women. Hormonal imbalances include elevated total testosterone (TT) levels, high luteinizing hormone/follicle stimulating hormone ratio (LH:FSH) along with metabolic derangements which include hyperinsulinemia, insulin resistance and deranged oral glucose tolerance test (OGTT). These patients are frequently obese, infertile, have irregular menses, have hirsutism and have a polycystic ovary on ultrasound. The cause of this pathology may be hyperinsulinemia or hyperandrogenism, however the exact cause is not known. Genes and environment are thought to play a role in the development of this disease. Its management includes treating menstrual irregularities, infertility, obesity, hyperinsulinemia and hyperandrogenism.[1]

There is much variation in the signs and symptoms of polycystic ovary syndrome but the Rotterdam criteria (2003) is used widely to diagnose PCOS. According to this criterion.

A patient must have two of the following to be diagnosed as having PCOS: 1) Evidence of hyperandrogenism (clinical or biochemical), 2) Anovulation or oligo-ovulation in the form of amenorrhoea or oligomenorrhoea, 3) Appearance of polycystic ovary on ultrasound.[1]

Despite a lot of research into the aetiology of this disease the exact cause of PCOS has not yet been found which is also the reason that this disease cannot be completely cured by pharmacological therapy.

Hyperandrogenism and resulting hyperandrogenaemia are thought to be the primary cause of PCOS. According to this theory the hypothalamic-pituitary-ovarian axis is defective causing increased secretion of LH. This acts on the LH receptors of the ovary and increases the activity of an enzyme called cytochrome P450c17α. This enzyme converts progesterone to androstenedione. Increased LH thus causes increased production of androstenedione which is converted to testosterone in the thecal cells via 17β reductase and is released into the blood. This androstenedione is also converted to oestradiol by FSH dependent aromatase enzyme in the granulosa cells of the ovary.[2] As in PCOS, LH levels are high as compared to FSH therefore androstenedione gets accumulated in the ovary. Androstenedione cause growth of the follicles in the early stages but persistence of its high levels retard the further growth of follicles into mature ones and hence ovulation does not occur resulting in the accumulation of antral follicles and the ovary becomes polycystic in appearance.[3] As there is no ovulation so cyclic menstruation is scanty or none at all. Increased levels of androgens in blood cause

clinical signs of hyperandrogenism like hirsutism, acne and androgenic alopecia etc.[4]

Hyperinsulinemia is also thought to be the cause of this syndrome. Most PCOS women are insulin resistant in part due to genetic predisposition and in part due to obesity and have deranged OGTT and BMI >25 kg/m$^2$. More than 50% women with PCOS are insulin resistant. In women with PCOS there is defective intracellular signalling after insulin binds to its receptors which cause decreased translocation of glucose transporters into the cell membrane. This in combination with glycogenolysis increases the blood glucose. This increases insulin secretion by the pancreas. This theory is supported by the fact that metformin, a biguanide that increases insulin sensitivity also improves metabolic, ovarian and androgen status in PCOS.[5]

The ovarian theca cells are responsible for the production of androgens and they do so under the control of LH via LH receptors. Insulin also stimulates the LH receptors and acts as a co-gonadotropin and hence hyperinsulinemia which is a prominent hallmark of PCOS also cause increased androgen production.[1] Ordinarily most of these androgens are transformed to oestrogens by the aromatase enzyme which is present in the granulosa cells and is under the influence of FSH. FSH levels are decreased as compared to the LH levels in PCOS so most of the androstenedione is converted to testosterone which cause hirsutism.[6] Hirsutism is the development of male type hair distribution in a female due to excess amount of androgens or male sex hormones which in turn results in change of vellus hair into terminal hair.[7]

The purpose of the study was to find out the gonadotropin levels of PCOS patients and compare them with the hormone levels of infertile patients without PCOS so as to rule out the common factor of infertility.

## MATERIAL AND METHODS

This cross-sectional study was conducted at Jinnahabad Medical Center from January to July 2013 over a period of six months. Blood samples were taken from the patients who were attending the gynaecology clinic at Jinnahabad Medical Center which is a private hospital in Abbottabad (Khyber Pukhtunkhwa). Ethical approval was granted by the Advanced Studies Research Board (ASRB) of Khyber Medical University. We selected 80 patients of which 40 had PCOS 40 without PCOs. Blood samples were taken and measurements were recorded in both groups at a single point of time.

Polycystic ovary syndrome was diagnosed on the bases of Rotterdam Criteria aging from 20 to 45. All patients were infertile, which was defined as: as per WHO guidelines stating that infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse." If a woman has never before given a live birth, then its primary infertility and secondary infertility is "the inability to get pregnant or give a live birth after previously getting pregnant and giving a live birth".[8] Patients with documented history of other co-morbidities like diabetes and hypertension and the use of hormones, smoking or drug abuse were excluded. Data was collected after informed consent.

History was taken from all the subjects with special emphasis on menstrual history, history of weight gain, abnormal hair distribution etc. Hirsutism was checked for by the Ferriman–Gallwey score**.** All the participants were subjected to an ultrasound scan by a trained lady doctor. Polycystic ovaries were checked for. Ovary was described as polycystic if there were ten or more cysts (2–8 mm in diameter) present peripherally, a dense stroma and enlarged ovary size > 10 cm$^3$.[9] Blood samples were taken in the early follicular phase of the menstrual cycle from all the patients included in the study. The blood samples were centrifuged and serum was separated. The sera were frozen and then tested for Luteinizing Hormone and Follicle Stimulating Hormone. The hormonal assays were carried out at the laboratory of Institute of Basic Medical Sciences (IBMS) Khyber Medical University, Peshawar on a machine called Chemiluminescence Immunoassay (CLIA) strip reader.

SPSS 19.0 was used for statistical analysis. The data showed a non-normal distribution. Mann-Whitney U test was carried out on the results to find out whether there was statistically significant difference between PCOs and Non-PCOs participants. $p$-value $\leq 0.05$ was taken as statistically significant.

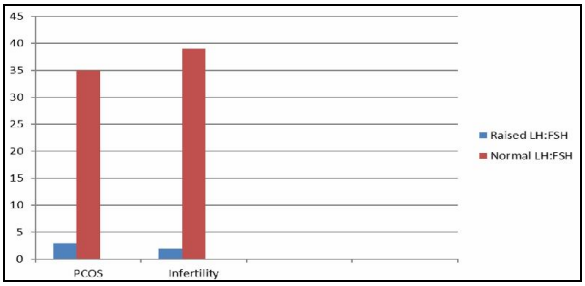


**Figure-1: LH:FSH ratio in patients with PCOS and in patients of infertility without PCOS**

## RESULTS

There were 40 participants each with PCO and 40 participants without PCO. The normal range for FSH in the follicular phase was 3–12.0 mIU/ml. FSH levels were raised in 12 out of 40 patients (30%) with PCOS and 7 out of 40 patients (17.5%) of no PCO. Mann-Whitney U test was applied which showed that there was no statistically significant difference between FSH values of the two groups (U=718.500, $p$=0.433)

The normal range of LH in the follicular phase of the menstrual cycle was from 0.5–10 mIU/ml. Three out of 40 (7.5%) had raised LH levels in participants with PCO, whereas among others it was 6 out of 40 (15%) that had raised LH levels. Mann-Whitney U test was applied which showed no significant difference between the two groups (U=773.5 and $p$-value=0.949).

LH/FSH ratios were calculated for both the groups. 1:1 is the normal ratio in a healthy female of reproductive age group. A ratio above >1 or >2 is taken as abnormal.[10] We took a cut-off value of above 1.35:1 as raised and this was looked for in PCO and non-PCO participants. LH:FSH was raised in 3 out of 35 patients (8%) with PCOs and 2 out of 39 patients (5%) in others. There was no statistically significant difference in the LH/FSH ratio of the two groups as indicated by applying Mann-Whitney U test (U= 522.500, $p$-value=0.083).

## DISCUSSION

In our study we assayed the levels of follicle stimulating hormone (FSH), luteinizing hormone (LH) and found the luteinizing hormone to follicle stimulating hormone ratio (LH:FSH) in PCOS cases and in the non-PCO participants comprising infertile patients without PCOS. In our study we found no statistically significant difference in the LH levels, FSH levels and the LH:FSH ratio between them. Contrary to this, another research stated that the levels of LH were raised in PCOS cases[11] and that LH:FSH ratio was also raised to 2:1 or 3:1.[12] However our findings were identical to a study which assayed the levels of gonadotropins in PCOS but did not find raised LH levels.[10] In another research LH:FSH ratio was found not to be raised in PCOS patients and of little diagnostic value in PCOS.[13]

In PCOS there is LH hypersecretion but the ovaries are also more sensitive to insulin and insulin augments the functions of LH. Insulin acts as a co-gonadotropin and causes increased production of androgens by the ovary possibly by causing the enzyme cytochrome P450c 17α to increase its 17α-hydroxylase activity. This part of the enzyme is under the control of LH and insulin potentiates the response of the enzyme to LH. The 17α-hydroxylase activity causes the production of androgens.[14] Thus even if the LH/FSH ratio is not increased as is the case of this study there can still be ovarian hypersecretion of androgens because of hyperinsulinemia or insulin resistance. A raised LH/FSH ratio however is a very strong indicator of PCOS.[15]

Limitations of our study are that it was on a small sample. Larger studies with case-control designs are required.

## CONCLUSION

In our study the LH to FSH ratio was not raised in majority of PCOS patients.

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## AUTHORS' CONTRIBUTION

MK: Research work, sampling, literature search, data collection, data analysis, study design, conceptualization, write-up. NS: Data interpretation, proof reading, study design, data analysis, write-up. RU: Data nalysis, data interpretation, proof reading. UK: Data collection, data analysis, data interpretation. UZ, HS: Data analysis, proof reading, write-up

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