



Frequency of Hyperprolactinemia in PCOS and its Association with Female Infertility

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ABSTRACT

Introduction: Infertility is a critical health concern partially due to intricacy in its causes and striving for its prevention, diagnosis and treatment. Various researches have documented a close linkage between polycystic ovary syndrome and hyperprolactinemia. **Aims & Objectives:** This study was aimed to determine the frequency of hyperprolactinemia in PCOS and its association with infertility in PCOS subjects. **Place and duration of study:** It was a cross sectional study, conducted during April 2017 and September 2017 at Aziz Fatimah Hospital, Faisalabad, Pakistan. **Material & Methods:** It was a cross sectional study which was conducted at Aziz Fatimah Hospital, Faisalabad, Pakistan from April to September 2017. This study comprised of 88 female subjects of 17-35 years old who included PCOS subjects and age matched controls. Hyperprolactinemia was assessed by the measurement of serum prolactin levels which were measured by chemiluminescence immunoassay technique (CLIA). SPSS version 22 was used for the statistical analysis of the data. **Results:** Out of total 88 female participants, 61.4% of polycystic ovary syndrome subjects had hyperprolactinemia as compared to this 36.4% of controls had hyperprolactinemia. Pearson correlation also revealed significant positive association of hyperprolactinemia with infertility. **Conclusion:** Hyperprolactinemia was frequently seen in polycystic ovary syndrome females as well as raised BMI was also found. Raised prolactin levels are strongly associated with female infertility.

Key words: Hyperprolactinemia, Infertility, Polycystic Ovary Syndrome.

INTRODUCTION

Infertility is a crucial problem, mainly affecting millions of parents worldwide.¹ It is one of the emerging problems associated with various genetic, medical, economic and psychological factors like anxiety, stress in both parents.² Infertility is the failure of a couple to conceive after one year of regular unprotected intercourse.³ It is categorized as primary infertility and secondary infertility. Primary infertility is the one in which a couple has never achieved a clinical pregnancy. In secondary infertility, there is difficulty to conceive after already being conceived³.

The frequency of infertility varies among different regions globally, hence affecting 5% to 8% in the developed countries and 5% to 44% in the developing countries.⁴ There are undeniable evidences that in Asian countries, infertility has become a major health concern.⁵ As in Pakistan, 22% of the couples are suffering from infertility. Among these 4% couples are having primary

infertility and 18% are suffering from the secondary infertility, eventually affecting one in every five married couples.³

Several factors have been associated with the female infertility, inclusive of age more than 35 years, late marriage, hormonal imbalances like thyroid disorders, diabetes mellitus, obesity, hypertension, history of having pelvic inflammatory disease and modern life style.³

Polycystic Ovary Syndrome (PCOS) and hyperprolactinemia being on the top of the list of the utmost common causes of infertility in women. PCOS is the most commonly identified endocrinopathy in females.^{1,6} The worldwide prevalence of the polycystic ovary syndrome is 3 to 15%.⁷ According to the Rotterdam Criteria, a female with two out of the following three characteristics is diagnosed as PCOS;

- 1- Oligo-ovulation or anovulation.
- 2- Clinical or biochemical signs of hyperandrogenism.
- 3- Polycystic ovaries.¹

Hyperprolactinemia is the frequent pituitary over secretion, both in men and women. It is hard to

identify hyperprolactinemia either due to the absence of specific clinical symptoms or due to the presence of ill-defined signs only.⁸

Ovulation is the essential requirement for conception.³ Oligo-ovulation or anovulation, menstrual disorders and the resulting infertility are the common features shared by PCOS and hyperprolactinemia. Conflicting results concerning association of PCOS with hyperprolactinemia were documented by various studies and exact relationship is still to be hypothesized.¹

There are various beliefs about the association of PCOS and hyperprolactinemia varying from the identification of raised prolactin levels being a characteristic of PCOS on one side, but on the other hand it is mandatory to exclude hyperprolactinemia while making a proper diagnosis of PCOS. There are many probable mechanisms which increase prolactin secretion which occurs in the polycystic ovary syndrome. Hyperprolactinemia might be the result of changed dopamine turnover which worsens the gonadotropin releasing hormone (GnRH) output, which in turn results in disturbed ovarian function establishing a shared basis for both PCOS and hyperprolactinemia.¹

This study was aimed to assess and compare prolactin levels in:

i) PCOS (infertile subjects) and control groups (fertile subjects) of study.

ii) Subjects with primary and secondary infertility. We also aimed to explore the association of hyperprolactinemia with PCOS and infertility.

Secondarily we also compare the BMI among PCOS and control groups as it is main contributing factor for PCOS.

MATERIAL AND METHODS

It was a cross sectional study conducted during April 2017 and September 2017 at Aziz Fatimah Hospital, Faisalabad, Pakistan. This study comprised of 88 females of age 17- 35 years, including polycystic ovary syndrome and controls, 44 subjects in each group. All subjects were enrolled from the outpatient department of gynecology and obstetrics by the non-probability purposive sampling technique. Polycystic ovary syndrome according to the Rotterdam criteria 2003 defined as a female having two out of the three features:

- 1- Oligomenorrhea or amenorrhea.
- 2- Hyperandrogenism (raised androgen levels)
- 3- Polycystic ovaries on ultrasound.⁹

Females with regular menstrual cycle, no signs of hyperandrogenism along with the normal appearing ovaries on ultrasound were taken as controls. Females who had any tumor of pituitary gland or with the previous history of neck and pelvic surgery were excluded. Females who were already taking medication for raised prolactin levels were excluded. The unwilling females were also excluded. Informed consent was taken from the females. A detailed history regarding menstruation and fertility was recorded on pre designed proforma. Anthropometric measurements were also taken. Weight in Kg and Height in meters were measured by stadiometer and used to calculate BMI. 4cc blood was taken under aseptic conditions and centrifuged it to separate serum. Serum was stored at -20°C in the pathology laboratory of Aziz Fatimah Hospital for further analysis. Serum Prolactin (PRL) was measured by chemiluminescence immunoassay technique (CLIA) by Maglumi Snibe 2000. The normal reference range for prolactin in females of reproductive age was taken as 66-490 µIU/ml (according to the kit manufacturers).¹⁰ Prolactin level greater than 490µIU/ml was considered as hyperprolactinemia.

Statistical analysis:

Analysis was done by using SPSS 22. Continuous variables like age, height, weight, BMI and prolactin levels were presented as mean ± standard deviation. Means were compared by t test between the study groups. Percentages are compared by chi square test (X^2). Pearson correlation was used to assess the association of hyperprolactinemia with infertility and PCOS.

RESULTS

Study comprised of 88 subjects, out of total 44 had PCOS and 44 were in control group. Mean age of participants was 26.2±3.65 years. Descriptive statistics of study population are described in Table-1. Out of total study population 25(28.4%) had primary infertility and 19(21.6%) had secondary infertility and 44 (50%) were fertile females. Fig-1 is showing comparison of serum prolactin between study groups. Serum prolactin levels were higher in PCOS as compared to control subjects with statistically significant difference (P-value 0.001*). BMI was significantly higher in PCOS group as compared to control group, (29.1±7.4 vs 21.6 ±105) with P value 0.000*. Fig-2 is revealing the comparison of serum prolactin levels among females with

primary and secondary infertility. Prolactin levels were higher in subjects with primary infertility as compared to secondary infertility, however no significant difference was found between them (P value 0.18). Out of total 44 PCOs, 27(61.4%) subjects have hyperprolactinemia, in contrast to this out of total 44 controls only 16 (36.4%) have hyperprolactinemia, rest of the population have normal prolactin levels. Pearson correlation reveals significant positive association of hyperprolactinemia with infertility (P value 0.030*) and PCOS (P-value 0.019*).

Anthropometric and Biochemical Statistics	Mean ± SD
Age (years)	26.2 ± 3.65
Height (m)	1.60 ± .080
Weight (kg)	64.5 ± 14.7
BMI (kg/m ²)	25.36 ± 6.55
Prolactin (μIU/ml)	524.4 ± 317.1

Table-1: Descriptive statistics of studied subjects (n=88)

SD= Standard Deviation, m= meter, Kg= kilogram, μIU/ml= micro international units per milliliter.

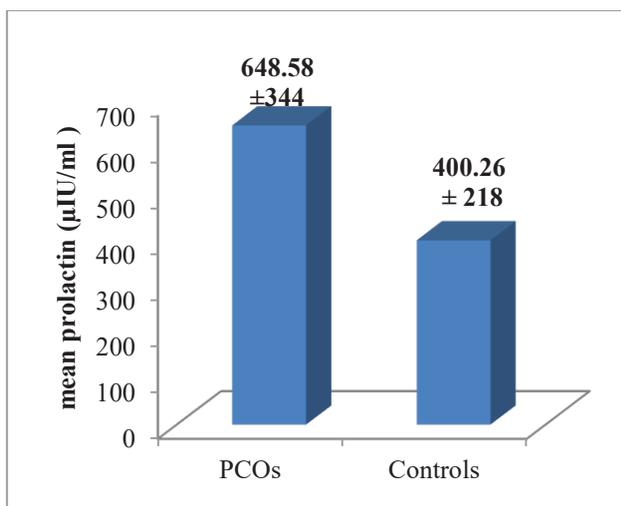


Fig-1: Serum Prolactin levels between PCOS and control group (n=88)

Means are compared by t-test. (P value=0.001*)

P value ≤ 0.05 was considered statistically significant

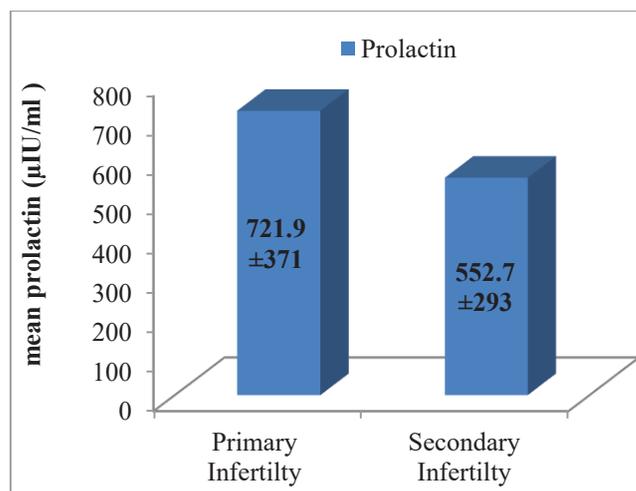


Fig-2: Comparison of serum prolactin levels between primary and secondary infertility (n=88)

Means are compared by t-test. (P value 0.18)

P value ≤ was considered statistically significant

DISCUSSION

Infertility is the biological inability of a couple to conceive and enjoy parenthood after unprotected intercourse over a period of at least 1-2 years. Infertility is emerging alarming problem globally because of social issues and associated psychological upsets likely to occur in both partners.² Polycystic ovary syndrome (PCOS) is one of the common and key contributor of the infertility. The prevalence of PCOS is rising at exponential proportions worldwide, in parallel with the ever increasing obesity.¹¹ Evidences are available documenting the association of hyperprolactinemia and PCOS but many researches on female infertility documented the conflicting results concerning this association.¹ Raised serum prolactin levels initiate the repression of hypothalamic pituitary axis and oppose the ovary to its gonadotropin activity, resulting in amenorrhea and absence of ovulation. Infertility linked with the raised prolactin levels is curable with treatment, regardless of the kind of treatment either medical or radical. Reducing the prolactin levels to the normal reference range is quite important for ovulation¹².

The present study was conducted to estimate the serum prolactin levels in subjects with polycystic ovary and to study the association hyperprolactinemia with infertility and PCOS. It comprised of total 88 subjects, out of which 44 subjects were studied as PCOs and 44 as control. Out of 44 PCOS subjects, 25 (28.4%) had primary infertility and 19 (21.6%) had secondary infertility. Interestingly, all the infertile subjects of

studied population were suffering from PCOS. Nallusamy et al, study conducted in India is in agreement with current result as they reported higher rates of primary infertility than secondary infertility (79.6% vs 20.4%).¹³

We also noted that the PCO subjects have higher BMI and majority were obese as compared to control subject subjects whose BMI was in normal range. Present study also found significant raised prolactin hormone in females suffering from PCOS and infertility as compared to controls fertile group (P-value 0.001*). These results are similar to the study done by Zina¹⁴ who found significant rise in serum prolactin levels in infertile females as compared to controls. As prolactin hormone impacts the ovaries either directly by decreasing the sensitivity of luteinizing hormone (LH) and follicle stimulating hormone (FSH) receptors in the ovaries or through the indirect action via reducing the secretion of gonadotropins (GnRH).¹⁴ In current study, 61.4% PCOS subjects have hyperprolactinemia as compared to this only 36.4% of control group had hyperprolactinemia. Various previous researches are in line with the results of current study and found significant raised prolactin levels in subjects with PCOS. Goswami and Shu et al found significant rise in serum prolactin levels in polycystic ovary syndrome.^{15,16} On contrary to the results of this study, previous studies conducted by Szosland et al and Oyebanji OG et al did not find any significant rise in prolactin levels in polycystic ovary syndrome as compared to controls.^{1,17} Significant prolactin elevation in patients with suspected PCOS should be investigated further to prevent the infertility.

CONCLUSION

Prolactin levels and BMI were higher in subjects with PCOS and infertility as compared to control group. Hyperprolactinemia is positively associated with PCOS and infertility.

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