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A hospital based study of hypothyroidism in polycystic ovarian syndrome in rural population of Gurugram, Haryana

Monu Sarin[1], Poonam Arora[2,*], SC Mohapatra[3]

[1]Associate Professor, Dept. of Radiodiagnosis & Imaging, [2]Assistant Professor, Dept. of Biochemistry, [3]Professor, Dept. of Community Medicine, Dean Academic Affairs, Faculty of Medical Sciences, SGT Medical College Hospital & Research Institute, Gurugram, Haryana

***Corresponding Author:**
Email: drpoonamarora2017@gmail.com

Abstract

Introduction: PCOS exists commonly among women in the reproductive age with an incidence rate of 6-10%.The clinical manifestations of PCOS include oligomenorrhoea, infertility, acne, hirsutism and obesity. There is a significant overlap of symptoms between PCOS and hypothyroidism.

Objective: The aim of this study is to investigate the prevalence of hypothyroidism in PCOS patients.

Materials and Method: This was a cross-sectional study of clinically diagnosed 50 females of PCOS and another 50 age matched female subjects were studied as the control population. PCOS and Hypothyroidism were diagnosed by Ultrasound (USG) and biochemical parameters T_3, T_4, TSH, LH, FSH and PRL.

Results: The mean TSH, LH, FSH, LH/FSH ratio and PRL are significantly higher in women with PCOS as compared to controls.

Conclusion: PCOS is on the rise in hypothyroid patients. Identification of hypothyroidism may help us to treat and prevent fertility complications in PCOS females. Hypothyroidism needs to be early corrected in the management of infertility associated with PCOS which is of major concern these days.

Keywords: Polycystic Ovarian Syndrome, Hypothyroidism, Thyroid Stimulating Hormone.

Introduction

In 1721 Antonio Vallisneri, an Italian scientist described for the first time the clinical & anatomo-pathological features of Polycystic Ovarian Syndrome (PCOS).[(1)] Since then PCOS has been one of the most discussed, controversial & studied areas of endocrine logical gynaecology. PCOS is a metabolic syndrome, characterized by anovulation, hyperandrogenism and polycystic ovary. PCOS exists commonly among women in the reproductive age with an incidence rate of 6-10%. The clinical manifestations of PCOS include oligomenorrhoea, infertility, acne, hirsutism and obesity. In addition these patients may develop many other endocrine related and metabolic diseases, and have increase risk of endometrial cancer, impaired glucose tolerance, diabetes, and cardiovascular disease.[(2)]

Elevated circulating androgen levels are observed in 80-90% of women with oligomenorrhoea as elevated levels of free testosterone account for the vast majority of abnormal findings in the laboratory examination.[(3)] It is important to understand that just because a women has multiple ovarian cysts doesn't mean that she has PCOS. The commonest criteria used for the diagnosis of PCOS these days is Rotterdam revised Criteria which includes any two of the following three features; 1) Oligo/anovulation 2) Clinical and/or biochemical evidence of hyperandrogenemia and 3) Ultrasonographic findings of Polycystic ovaries; with exclusion of other known disorders of hyperandrogenemia.[(4,5)]

Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of the endocrine gland. Abnormalities in the supply of thyroid hormone to the peripheral tissue are associated with alteration in a number of metabolic processes. Infantile hypothyroidism if untreated, leads to sexual immaturity. Untreated juvenile hypothyroidism causes a delay in the onset of puberty followed by anovulatory cycles. In adult women, severe hypothyroidism may be associated with diminished libido and failure of ovulation. Primary ovarian failure can also be seen in patients with Hashimoto's thyroiditis as a part of autoimmune polyglandular syndrome. Rarely, in primary hypothyroidism, secondary depression of pituitary function may lead to ovarian atrophy and amenorrhoea.[(6)]

Hypothyroidism is an underactive thyroid is a frequent cause of infertility. If the thyroid is underactive, the hypothalamus and pituitary gland can sense this and try to kick things back to normal by increasing levels of the hormones TRH (thyroid releasing hormone) and TSH (thyroid stimulating hormone). TRH produced by the hypothalamus, prompts the pituitary to release TSH, which in turn stimulates the thyroid to do its job. However, TRH also prompts. Elevation of prolactin can interfere with ovulation by suppressing release of the hormones LH and FSH, which stimulate the ovary. Low levels of thyroid hormone can also interfere with the metabolic clearance rate of sex hormones, which can also cause ovulatory disorders.[(7)] Early stages of thyroid

dysfunction (before symptoms are manifest) can lead to subtle changes in ovulation and endometrial receptivity, which then may have profound effects on fertility.[8] Thyroid hormones interact with reproductive hormones, estrogens, progesterone, to prevent normal function of the ovaries and maturation of the egg.[9]

Materials and Method

The study was carried out in the Department of Radiodiagnosis and Department of Biochemistry, SGT Medical College, Budhera, Gurugram, Haryana. This case controlled study enrolled 50 women with PCOS. All women in age group 20-45 years attending outpatient in the department of Obstetrics & Gynaecology at SGT Medical College, Hospital & Research Instituite, Gurugram, Haryana with the primary complaints of menstrual irregularities (amenorrhoea or oligomenorrhoea) and/or hirsutism with or without infertility were evaluated in detail for polycystic ovarian syndrome.

A total of 50 newly diagnosed PCOS patients were compared with 50 age and sex matched normal healthy controls. A written informed consent was also taken from the cases with detailed history**.** The participants had pelvic ultrasound scan with full bladder, and those found to have ultrasound criteria of PCOS were included in the final group. The evaluated ultrasound criteria of diagnosis of polycystic ovaries were the presence of multiple (more than 12 in number) small peripherally arranged 2-9mm ovarian follicles (string of pearls) around the highly echogenic ovarian stroma with enlarged ovaries (volume >10 cm^3).

Transabdominal ultrasound was performed between 2nd to 10th day of the mentrual cycle or during any day of amenorrhoea using 3.5-5 MHz curved-array transducer on Toshiba Nemio XG & Philips Affiniti 50 USG machine. Ultrasound was done in full bladder with optimized gain settings depending upon the amount of pelvic fat. Ovarian measurements were taken & volume was assessed. Transvaginal USG (TVS) is preferred over transabdominal USG because of better resolution & patients' preference as the need for full bladder is avoided. TVS was done in willing patients with high frequency probe (7.5-10 MHz). The ultrasound criteria of 12 or more follicles measuring 2-9mm was the commonest finding observed in patients followed by peripheral distribution of follicles.

USG of thyroid gland was done using high frequency 5-7.5 MHz linear transducer. Thyroid gland was analyzed for its size, echogenicity or any focal nodule & its vascularity. Goiter (enlargement of thyroid gland) was included as 20mm inclusion criteria. Venous blood samples were obtained in the follicular phase from all the patients and analyzed for biochemical parameters T_3, T_4, TSH, LH, FSH and PRL. All parameters were quantitatively estimated in serum by using SEIMENS-Centaur CP analyzer based on chemiluminescent immuno assay (CLIA).

Results

The present study was conducted on 50 patients of PCOS in the age group of 20-45 years. PCOS was diagnosed in these patients according to Rotterdam criteria of PCOS. Several clinical characteristics and biochemical parameters were compared among the patients and a control group of age matched healthy women. In our study maximum number of PCOS patients were in the age group of 20-25 years (23 patients, 46%), followed by 26-30 years (14 patients, 28%).

As compared to controls, PCOS patients showed significant increase in mean TSH levels (2.13± 0.85 vs 5.23± 1.93, p<0.0001), and slight decrease in serum T_4 levels (7.42± 2.96 vs 5.98± 3.23, p<0.001) while serum T_3 levels showed no significant difference (1.58± 0.27 vs 1.61±0.38, p= 0.008). Also mean LH & FSH levels were significantly higher in PCOS patients (5.8± 2.10 vs 19.6.± 6.79, p<0.0001 and 5.03 ± 2.41 vs 7.18± 2.87). The LH/FSH ratio was also elevated above 2.0 in 41 patients (82.5%). Serum Prolactin (PRL) levels (10.45± 4.67 vs 28.76± 9.98, p<0.0001) were also significantly increased in the patients of PCOS. (Table 1)

Table 1: The comparison between serum hormonal levels in healthy controls and PCOS patients

Biochemical Parameters	Control (n=50) Mean± SD	PCOS (n=50) Mean± SD
T_3 (0.4-2.01 ng/ml)	1.58± 0.27	1.61±0.38
T_4 (4.5-11 µg/dl)	7.42± 2.96	5.98± 3.23
TSH (0.4-4.5 mIU/ml)	2.13± 0.85	5.23± 1.93
LH (1.7-15 mIU/ml)	5.8± 2.10	19.6.± 6.79
FSH (1.2-8 mIU/ml)	5.03 ± 2.41	7.18± 2.87
LH/FSH Ratio	1.15	2.72
PRL(3.8-23 ng/ml)	10.45± 4.67	28.76± 9.98

Discussion

Thyroid hormones have various effects on the reproductive system of the human female. Alteration in thyroid function, particularly hypothyroidism, can cause ovulatory dysfunction and lead to impaired female fertility. Hypothyroidism and PCOS are often accompanied by increased serum free testosterone, luteinizing hormone (LH) and high cholesterol levels. When the ovaries of hypothyroid women with PCOS are viewed with an ultrasound an increase in ovarian volume and the appearance of bilateral multicystic ovaries are often visible. When thyroid hormone replacement therapy is initiated, in addition to

stabilizing thyroid hormone levels, ovarian cysts regress and ovarian volume is reduced.[10]

Hypothyroidism led to lowering of sex hormone binding globulin level and increment of testosterone level but not invariably directed towards estriol overproduction.[11] Hypothyroidism worsens PCOS by further decreasing sex hormone binding globulin levels, increasing the conversion of androstenedione to testosterone and aromatization to estriol and reducing the metabolic clearance rates of androstenedione and estrone. Since thyroid hormones are involved in the gonadotropin induced estradiol and progesterone secretion by human granulosa cells, hypothyroidism would interfere with ovarian function and fertility.[12]

In our study PCOS is maximum in 20-25 years of age group followed by 26-30 years and has decreased significantly after 30 years. This may be due to the fact that menstrual symptoms begin from puberty itself which leads to early presentation in the OPD. These findings are supported by another study done by Sinha et al.[6]

In the present study we found that in PCOS patients elevated TSH indicates the subclinical hypothyroidism and LH/FSH ratio was also elevated above 2.0 in 41 patients (82.5%). This has been also seen in other studies.[10,12,13,14] We also observed that PRL levels were also higher in women with PCOS when compared to controls, which is concordant with various studies.[15,16] Hyperprolactinemia is a major cause of subfertility, and treatment with drugs which lowers PRL levels showed that 24% infertile women became pregnant.[17]

Hence, prevalence of subclinical hypothyroidism is higher in females with PCOS. The pathophysiology and various contributing factors for the association of these two diseases are yet to be elucidated. So, the women with PCOS in reproductive age group adversely affected by associated thyroid dysfunction and both pose risks of ovarian failure and pregnancy related complications.

Conclusion

It has been observed that PCOS is on the rise in hypothyroid patients. Identification of hypothyroidism may help us to treat and prevent fertility complications in PCOS females. Hypothyroidism needs to be early corrected in the management of infertility associated with PCOS which is of major concern these days.

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