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Original research article

A cross-sectional study to investigate the prevalence and etiology of different thyroid disorders in PCOS patients

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Abstract

Background: Polycystic ovarian syndrome (PCOS), the most common endocrinopathy of women in the reproductive age group seems to be adversely affected by associated thyroid dysfunction. Both pose independent risks of ovarian failure and pregnancy related complications.

Aim: to investigate the prevalence and etiology of different thyroid disorders in PCOS patients.

Material and methods: This cross-sectional study conducted in Anugrah Narayan Magadh Medical college and Hospital, Gaya, Bihar, India, for 12 months. Total 80 female patients in the age group between 18 and 35 years, diagnosed of PCOS were included in the study. Diagnosis of PCOS was done by Rotterdam classification. Hirsutism was graded by Ferriman–Gallwey score. Based on this score pattern and other clinical tests, hirsutism can be evaluated as mild, moderate or severe. Fasting blood sugars, fasting insulin levels, serum luteinizing hormone (LH), follicle stimulating hormone (FSH), TSH, serum testosterone, dehydroepiandrosterone, and serum prolactin were done. **Results:** The mean age of the patients with PCOS was 21.5±4.77 years. All the patients had some form of menstrual irregularities either oligo menorrhea, irregular menses or secondary amenorrhea. A total of 60(75%) had body mass index ≥25 kg/m. Clinical hirsutism was present in significant number 72.5% of cases (Ferriman–Gallwey score >7). LH/FSH ratio of more than 2 was found in 62.5% of the cases. Homeostatic model assessment IR (HOMA-IR) was calculated from fasting blood sugar and fasting insulin levels, and 56 subjects (70%) were insulin resistant. The mean TSH levels in subjects were 4.39±1.91.

Key words: autoimmune thyroiditis, hypothyroidism, polycystic ovarian syndrome

Introduction

Polycystic ovarian syndrome (PCOS), also known as Stein and Leventhal syndrome, is one of the most common female endocrine disorders with a prevalence of 5%–10% in women of reproductive age group. It is a complex disorder wherein numerous genetic variants and environmental factors combine and contribute to the pathogenesis.[1] PCOS is of both clinical and public health importance, and its prevalence has recently been shown up to 18% in premenopausal women with current Rotterdam diagnostic criteria.[2] The increased prevalence of obesity and metabolic syndrome in the general population is contributing to the increased burden of PCOS in our society.[3] Thyroid disorders are arguably the most common endocrine disorder worldwide. In two large studies from India, the prevalence of antithyroid peroxidase antibody (TPO Ab) positivity, overt hypothyroidism, and subclinical hypothyroidism has been

reported to be 13.3%–21.8%, 3.5%–4.2%, and 8.02%–19.3%, respectively.[4-6] Although the etiopathogenesis of hypothyroidism and PCOS is completely different, these two disorders have many features in common. Thyroid disorders can be associated with menstrual disturbances and infertility, which are also common symptoms in PCOS. An increase in ovarian volume as well as cystic changes in the ovaries has been reported in primary hypothyroidism.[7] Mildly raised prolactin has been observed in PCOS. Raised prolactin levels have been documented in children and adults with mild subclinical hypothyroidism, which may also contribute to the overlapping features of menstrual irregularity seen both in hypothyroidism and PCOS.[8,9] Few studies have shown that thyroid disorders are more common in women with PCOS as compared to the normal population.[10-12] Routine screening for thyroid dysfunction in hyper androgenic patient is of little value since the incidence of these disorders is not higher in hyper androgenic patients than in normal women of child bearing age.[13] With this background, the present study has been contemplated to investigate the prevalence and etiology of different thyroid disorders in PCOS patients attending a tertiary care hospital.

Material and methods

This cross-sectional study conducted in the Department of Pharmacology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India, for 12 months, after taking the approval of the protocol review committee and institutional ethics committee. total 80 female patients in the age group between 18 and 35 years, diagnosed of PCOS were included in the study. The patients on oral contraceptives or hormone replacement therapy, liver and kidney diseases, congenital adrenal hyperplasia simple virilising or severe, adrenal insufficiency, Cushing's syndrome, primary amenorrhea due to any cause, Sheehan syndrome, pregnancy, lactation, treatment for infertility, premature ovarian failure, and hyperprolactinemia were excluded.

Treatment naïve patients meeting inclusion-exclusion criteria were recruited for the study. A through clinical examination and history was taken. Menstrual history noted. Diagnosis of PCOS was done by Rotterdam classification (Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met: Oligo ovulation and/or anovulation, excess androgen activity [clinical and or biochemical] and polycystic ovaries (by gynecologic ultrasound multiple cysts more than 2 in number of 2-9 mm size]). Hirsutism was graded by Ferriman–Gallwey score. Based on this score pattern and other clinical tests, hirsutism can be evaluated as mild, moderate or severe.

Another relevant history about symptoms of hyper/ hypothyroidism was asked. History of primary or secondary infertility was asked. The patients were asked to report in fasting state for the following investigations: Fasting blood sugars, fasting insulin levels, serum luteinizing hormone (LH), follicle stimulating hormone (FSH), TSH, serum testosterone, dehydroepiandrosterone, and serum prolactin were done. FSH and LH were done on the 2nd or 3rd day of menstrual cycle. Gynecological ultrasound was done to assess ovarian condition and presence or absence of multiple cysts.

Results

80 patients met the diagnostic criteria of PCOS. The mean age of the patients with PCOS was 21.5±4.77 years. All the patients had some form of menstrual irregularities either oligo menorrhea, irregular menses or secondary amenorrhea. A total of 60(75%) had body mass index ≥25 kg/m. Clinical hirsutism was present in significant number 72.5% of cases (Ferriman–Gallwey score >7) Table 1. LH/FSH ratio of more than 2 was found in 62.5% of the cases. Homeostatic model assessment IR (HOMA-IR) was calculated from fasting blood sugar and fasting insulin levels (Table 1), and 56 subjects (70%) were insulin resistant.

The mean TSH levels in subjects were 4.39±1.91. The distribution of thyroid dysfunction among subjects. Subclinical hypothyroidism was seen in 20(25%) cases and overt

hypothyroidism in 17 (21.25%) cases (Table 3). Total thyroid dysfunction (clinical and subclinical) was seen in 37(46.25%) cases. Thyrotoxicosis and multinodular goiter was not seen in our study.

Table 1: Demographic profile of PCOS patients

Demographic profile	PCOS (n=80)
Age (years)	21.5±4.77
BMI (kg/m2)	27.12±4.62
Hirsutism	58 (72.5%)
Ferriman–Gallwey score	17±5.22
Serum testosterone (ng/ml)	22.53±55.62
Serum DHEAS (ug/ml)	3.57±1.73
Fasting sugar (mg/dl)	89.29±12.09
Fasting serum insulin (ulU/ml)	23.11±8.36
HOMA-IR	3.69±2.88
LH (mIU/ml)	13.11±5.74
FSH (mIU/ml)	5.78±2.42
PRL (ng/ml)	6.84±4.53

PCOS: Polycystic ovarian syndrome, BMI: Body mass index, HOMA-IR: Homeostatic model assessment insulin resistance, DHEAS: Dehydroepiandrosterone-sulfate, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, PRL: Prolactin

Table 2: Thyroid function tests in PCOS

Investigations	Number of patients n=80
fT3 (pg/ml)	2.98±1.63
fT4 (ng/dl)	1.69±1.22
TSH (mIU/ml)	4.39±1.91

Raised serum testosterone was found in 64% of the cases. PCOS: Polycystic ovarian syndrome

Table 3: Various thyroid abnormalities in patients with PCOS

Thyroid abnormalities	PCOS (n=80) (%)
Goiter	5 (62.5)
Subclinical hypothyroidism	20 (25)
Overt hypothyroidism	17 (21.25)
Grave's disease	Nil
Multinodular goiter	Nil

Discussion

Our study reports a high percentage of thyroid dysfunction in subjects with PCOD. We found that 46.25% of the cases have either clinical 17(21.25%) or subclinical 20(25%) hypothyroidism. Although hyperthyroidism was not seen in any of the case. The overall percentage of thyroid dysfunction among females in general population has been shown to be around 11.4% in an epidemiological study from India.[14] Many other studies have reported a very high percentage of thyroid dysfunction in PCOS cases.[15,16] Sinha et al. have reported 22.5% subclinical hypothyroidism and clinical hypothyroidism in 2.5% the findings of which are very close to our study. Janssen et al. observed a high percentage of autoimmune thyroid dysfunction in PCOS though in our study we have not looked at the autoimmune nature of thyroid dysfunction.

Researchers suggest an increased estrogen and estrogen/ progesterone ratio to be directly involved in high anti-thyroid peroxidase levels in PCOS patients.[16] Both genetic and environmental factors are believed to be contributing to thyroid disorders in PCOS. Hypothyroidism is known to cause PCOS-like ovaries and overall worsening of PCOS and IR.[17,18] Estrogen's immune stimulatory activity is normally countered by anti-inflammatory actions of progesterone levels of which are near zero in PCOS because of an ovulatory cycles. As a result immune system is over- stimulated resulting in autoimmunity and high incidence of autoimmune thyroid dysfunction.[19] Ghosh et al. did comparative analysis and suggested that hypothyroidism led to lowering of sex hormone-binding globulin levels and increment of testosterone levels.[20] All our patients had some form of menstrual problem ranging from oligo menorrhea, irregular menses to secondary amenorrhea. This matches with other studies in which menstrual irregularities were observed from 60% to 93%.[16,21,22] High incidence of obesity and IR as measured by HOMA-IR in our study is also similar to findings of others.[16,22] We report LH/FSH ratio of more than 2 in 62.5% of the cases. Sinha et al. and Anwary et al. have found this high LH/FSH ratio in 55% and 56%[16] while Anlakash.[23] has reported this to be 64%. A hypothesis has been established that hypothyroidism worsens PCOS by decreasing sex hormone binding globulin levels, which increases conversion of androstenedione to testosterone and reduction in metabolic clearance rate of androstenedione and estrone. Since thyroid hormones in gonadotropin-induced estradiol and progesterone secretion by granulose cells, hypothyroidism may interfere with ovarian function and fertility.[24]

Conclusions

High prevalence of thyroid disorders in PCOS patients thus points towards the importance of early correction of hypothyroidism in the management of infertility associated with PCOS.

Reference

1. Fritz MA, Speroff L. Clinical Gynaecolgic and Endocrinology and Infertility. 8thed. New Delhi: Wolter Kluver India Pvt., Ltd.; 2011.
2. Diamanti-Kandarakis E, DunaifA. Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. Endocr Rev 2012;33:981-1030.
3. Devru N, Dharmshaktu P, Kumar G, Dutta D, KulshreshthaB. Phenotypic presentation of adolescents with overt primary hypothyroidism. J Pediatr Endocrinol Metab 2018;31:415-20.
4. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocrinol Metab 2013;17:647-52.
5. Marwaha RK, Tandon N, Ganie MA, Kanwar R, Sastry A, Garg MK, et al. Status of thyroid function in Indian adults: Two decades after universal salt iodization. J Assoc Physicians India 2012;60:32-6.
6. Kalra S, Kumar A, Jarhyan P, Unnikrishnan AG. Indices of thyroid epidemiology. Indian J Endocrinol Metab 2015;19:844-7.
7. Khandelwal D, Tandon N. Overt and subclinical hypothyroidism: Who to treat and how. Drugs 2012;72:17-33.
8. Sharma LK, Sharma N, Gadpayle AK, Dutta D. Prevalence and predictors of hyperprolactinemia in subclinical hypothyroidism. Eur J Intern Med 2016;35:106-10.
9. Sharma N, Dutta D, Sharma LK. Hyperprolactinemia in children with subclinical hypothyroidism. J Clin Res Pediatr Endocrinol 2017;9:350-4.
10. Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN, Pal SK. Thyroid disorders in polycystic ovarian syndrome subjects: A tertiary hospital based cross-sectional study from Eastern India. Indian J Endocrinol Metab 2013;17:304-9.

11. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol 2004;150:363-9.
12. Kachuei M, Jafari F, KachueiA, KeshteliAH. Prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Arch Gynecol Obstet 2012;285:853-6.
13. Balen AH, Anderson RA, Policy & Practice Committee of the BFS. Impact of obesity on female reproductive health: British Fertility Society, Policy and Practice Guidelines. Hum Fertil (Camb) 2007;10:195-206.
14. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15 Suppl 2:S78-81.
15. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol. 2004;150(3):363-9.
16. Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN, Pal SK. Thyroid disorders in polycystic ovarian syndrome subjects: A tertiary hospital based cross-sectional study from Eastern India. Indian J Endocrinol Metab. 2013;17(2):304-9
17. Yildiz BO, Bolour S, Woods K, Moore A, Azziz R. Visually scoring hirsutism. Hum Reprod Update. 2010;16(1):51-64.
18. Garelli S, Masiero S, Plebani M, Chen S, Furmaniak J, Armanini D, et al. High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2013;169(2):248-51.
19. Angstwurm MW, Gärtner R, Ziegler-Heitbrock HW. Cyclic plasma IL-6 levels during normal menstrual cycle. Cytokine. 1997;9(5):370-4.
20. Ghosh S, Kabir SN, Pakrashi A, Chatterjee S, Chakravarty B. Subclinical hypothyroidism: A determinant of polycystic ovary syndrome. Horm Res. 1993;39(1-2):61-6.
21. Carmina E, Lobo RA. Treatment of hyperandrogenic alopecia in women. Fertil Steril. 2003;79(1):91-5.
22. Najem F, Elmehdawi R, Swalem A. Clinical and biochemical characteristics of polycystic ovary syndrome in Benghazi - Libya; A Retrospective study. Libyan J Med. 2008;3(2):71-4.
23. Anlakash AH. Polycystic ovarian syndrome - The correlation between LH/FSH ratio and disease manifestation. Middle East Fertil Soc J. 2007;12(1):35-40.
24. Wakim AN, Polizotto SL, Burholt DR. Augmentation by thyroxine of human granulosa cell gonadotrophin-induced steroidogenesis. Hum Reprod. 1995;10(11):2845-8.

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