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THYROID PROFILE OF POLYCYSTIC OVARIAN SYNDROME CASES IN A TERTIARY CARE HOSPITAL: A PROSPECTIVE OBSERVATIONAL STUDY.

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ABSTRACT **Introduction**–PCOS is a spectrum of disease commonly manifest as menstrual irregularity, acne and hirsutism. Clinical manifestations including menstrual irregularities and impaired fertility is the results of anovulation and/or luteal phase defect is shared by both PCOS and hypothyroid women. We aim to find out the incidence of hypothyroid in women with PCOS and to study the effect of hypothyroid and PCOS on different clinical parameter.

Materials and methods- The study was conducted as a prospective observational study on 183 cases of PCOS who attended the OPD of VIMSAR, Burla, India, with the objective of finding the prevalence of hypothyroidism in PCOS and to determine the association between hypothyroidism and various clinical and laboratory parameters in PCOS.

Results- The mean age of patients with PCOS was 25.896 ± 4.69 years. Women with PCOS presented with menstrual irregularity 158/183(86.34 %), hyperandrogenism in 147/183(80.33%) and 43/183(68.25%) presented with infertility. Acne, Acanthosis Nigricans and Hirsutism was seen in 65/183(35.52%), 29/183(15.85) and 55/183(30.06%) respectively. 69/183(37.70%) of cases had insulin resistance. When patients were tested for thyroid abnormality, 25(13.66%) found to have hypothyroidism, 2 (1.09%) had hyperthyroidism and 156(85.25%) had normal thyroid function. Patitents with PCOS with hypothyroidism had significantly increase incidence of acne, acanthosis nigricans, hirsutism, insulin resistance and high BMI ($p<0.005$).

Conclusion- As the features of both PCOS and hypothyroidism are overlapping and an association between these two disease states is not uncommon , thyroid profile should be analyzed which may help in better understanding of the etiology and management of PCOS.

KEYWORDS : acanthosis nigricans; insulin resistance; hirsutism, menstrual irregularity; polycystic ovarian syndrome; thyroid function test

Introduction-

PCOS is one of the most common endocrinopathies affecting 4-7% of women in the reproductive age group[1] and contribute to a major share of anovulatory infertility. It is more prevalent in South Asian woman than in Caucasians[2], though it can present in women of any ethnicity. The current diagnostic criteria for PCOS are the 2003 Rotterdam ESHRE/ASRM revised consensus[3].

The features of both PCOS and hypothyroidism are overlapping and an association between these two disease states is not uncommon.[4] Approximately 99.97% of T_4 and 99.7 % of T_3 is in bound form and only a small fraction of these hormones circulate unbound and is free for biological activity. Thus, to reach the actual diagnosis and to assess the thyroid function, free fraction of these hormones is essential. Therefore, this study is to estimate and analyse the correlation between hypothyroidism and PCOS.

Material and methods-

Type of study– The study was conducted amongst patients attending the OPD of department of Obstetrics and Gynaecology at VIMSAR, Burla, India, from October 2014 to October 2016. It was a prospective observational study to find the prevalence of hypothyroidism in PCOS patients and also to determine the association between clinical and laboratory parameters of PCOS with hypothyroidism. The study was conducted in 183 cases of PCOS who attended the outpatient department from October 2014 to October 2016.

Inclusion criteria-

PCOS patients (Diagnosed by USG pelvis and clinical examination) attending outpatient department of Obstetrics and Gynaecology, VIMSAR, Burla.

Exclusion criteria-

1. Congenital Hypothyroidism.
2. Thyroidectomy patients.
3. History of radiation to head and neck in cancer patients.
4. Women who are not willing for examination and further investigations and follow up.

On the first visit details history of the women was taken. Her age, parity, menstrual history, obstetric history, past medical history was taken. A comprehensive general and systemic examination was carried out. They were investigated with LH, FSH, TSH, Free T3, Free T4, Fasting Insulin, and USG Pelvis. TFT including TSH, Free T3, and free T4 was estimated using chemiluminescence method. According to this, TSH normal range was taken as 0.34-4.25 µIU/ml, free T3 normal range was 2.4-4.2 pg/ml (3.7-6.5 pmol/L), free T4 normal range was 0.7-1.24 ng/dl (9.0-16 pmol/L).[5] TSH above 4.25µIU/ml, free T3 below 2.4 pg/ml and free T4 below 0.7ng/dl was considered as overt hypothyroidism and high TSH with normal free T3 and free T4 are considered as subclinical hypothyroidism.

Ethical statement- The study was approved by the ethical committee of the hospital. The aim of the study was explained appropriately and informed written consent was obtained from all the patients.

Results- This prospective observational study aimed to analyse the correlations between the PCOS and thyroid abnormality. Details of baseline demographic parameters of patients with PCOS were summarized in table-1. Out of 183 cases studied 84(45.9%) belonged to 15-25 years, 88(48.09%) belonged to 26-35 years and 11(6.01%) belonged to 36-45 years. The mean age at presentation was 25.89 ± 4.69 years. In the present study majority of patients were either belong to upper middle class 79(43.17%) or lower middle class 75(40.98%). They mostly presented with menstrual problem (Oligomenorrhea, Polymenorrhea, and Secondary amenorrhea) in 158/183(86.34%), hyperandrogenism (Acne, Hirsutism) in 147/183(80.33%) and 43/183(68.25%) had infertility. Clinical features with PCOS patients are concisely tabulated in table 2. Out of 183 cases of PCOS, 40(21.86%) had secondary amenorrhea, 114(62.29%) had oligomenorrhea, 4(2.19%) had polymenorrhea and 25(13.66%) had normal cycle. Patients presented with infertility, 36(83.72%) had primary infertility and 7(16.28%) had secondary infertility. The mean duration of infertility was 1-2 years in 14(32.56%), 25(58.14%) had 3-

5 years and 4(9.3%) had more than 5 years of infertility. Most of the patients were overweight 95(51.91%) or obese 22(12.02%). Mean body mass index (BMI) was 25.676 ± 2.768 Kg/m2. Eight (4.37%) of PCOS patients were hypertensive. Of 128 cases of PCOS with hirsutism, 87(67.97%) had mild hirsutism, 39(30.47%) had moderate hirsutism and 2(1.56%) had severe hirsutism. Acne and acanthosis nigricans was seen in 65(35.52%) and 29(15.85%) of patients respectively. Mean fasting serum insulin was 17.065 ± 8.1184 µIU/ml; with fasting serum insulin ≥ 20 µIU/ml (hyperinsulinemia) was seen in 69(37.705%) patients. Patients with FBS/Fasting serum insulin ratio < 4.5 (Insulin resistance) was seen in 69(37.705%) patients and 114(62.295%) had FBS/Fasting serum insulin ratio ≥ 4.5. When patients were tested for thyroid abnormality, 25(13.66%) found to have hypothyroidism, 2 (1.09%) had hyperthyroidism and 156(85.25%) had normal thyroid function. Mean TSH, free T3 and free T4 was 2.73 ± 1.53 µIU/ml, 3.19 ± 0.4898 pg/ml. and 1.044 ± 0.19 ng/ml respectively. Subclinical hypothyroidism was seen in 14(56%) patients and overt hypothyroidism constitutes 11(44%) of cases. Menstrual irregularities including oligomenorrhea and secondary amenorrhea were the major symptoms in 24 (96%) of hypothyroid patients. Percentage of patients with menstrual irregularities were more in PCOS with hypothyroidism compared to PCOS without hypothyroidism, but the two tailed 'p' value equals 0.081(>0.05)which was statistically not significant. Details comparison of menstrual irregularities, hyperandrogenisim, and acanthosis nigricans among PCOS with or without thyroid abnormality is summarized in table 3. Out of 25 cases of PCOS with hypothyroidism, 24 (96%) had features of hyperandrogenism and 123(77.85%) PCOS without hypothyroidism, had features of hyperandrogenism with a p value of 0.034(<0.05). Acanthosis nigricans was seen in 20(80%) of hypothyroid with PCOS and 9(5.7%) of PCOS without hypothyroid with a p value of 0.001. PCOS with hypothyroidism more prone to have increased BMI 22(88%) (Overweight and Obese) compared to 95(60.13%) of PCOS without hypothyroidism (p value 0.007). So, the association is considered to be statistically significant. When we have compared insulin resistance among PCOS patients with or without hypothyroidism, we find a statistically significant difference between the two groups (p value <0.001).

Tables

Table1- Demographic characteristics of patients with pcos

parameters	N (percentage)
Age Distribution (Years)	
15-25	84/183(45.9)
26-35	88/183(48.09)
36-45	11/183(6.01)
Socioeconomic status	
Upper High	1/183(0.55)
High	2/183(1.09)
Upper Middle	79/183(43.17)
Lower Middle	75/183(40.98)
Poor	26/183(14.21)
Fertility Status	
Infertile	43/63(68.25)
No infertility	20/63(31.75)
Type of Infertility	
Primary Infertility	36/43(83.72)
Secondary Infertility	7/43(16.28)
Duration of infertility	
1-2 years	14/43(32.56)
3-5 years	25(58.14)
>5 years	4/43(9.3)
BMI(Kg/m2)	
<18.5(Underweight)	2/183(1.1)
18.5-24.9(Normal)	64/183(34.97)
25-29.9(Over weight)	95/183(51.91)
≥ 30(Obese)	22/183(12.02)
Blood Pressure	
Hypertensive	8/183(4.37)
Normotensive	175/183(95.63)

Table 2 Clinical features of patients with pcos

Parameter	N/ percentage
Chief Complaints	
Menstrual complaints	158/183(86.34)
Hyperandrogenism	147/183(80.33)
Infertility	43/183(68.25)
Menstrual Complaints	
Secondary Amenorrhea	40/183(21.86)
Oligomenorrhea	114/183(62.29)
Polymenorrhea	4/183(2.19)
Normal	25/183(13.66)
Distribution of Hirsutism	
Present	128/183(69.94)
Absent	55/183(30.06)
Type of Hirsutism	
Mild	87/183(67.97)
Moderate	39/183(30.47)
Severe	2/183(1.56)
Distribution of Acne	
Presence of Acne	65/183(35.52)
Absence of Acne	118/183(64.48)
Acanthosis Nigricans	
Present	29/183(15.85)
Absent	154(84.15)
Serum Insulin	
Fasting (≥ 20µIU/ml)	69/183(37.70)
Fasting (<20µIU/ml)	114/183(62.29)
FBS/Serum Insulin	
< 4.5	69/183(37.70)
≥ 4.5	114/183(62.29)
Hypothyroidism	25(13.66)
Hyperthyroidism	2(1.09)
Normal TFT	156(85.25)
Type of Hypothyroidism	
Subclinical hypothyroidism	14(56)
Overt hypothyroidism	11(44)

Table 3 -comparison of clinical features among pcos patients with or without hypothyroidism

Parameter	PCOS with hypothyroidism	PCOS without hypothyroidism	P value
Menstrual irregularities	24(96%)	130(82.28%)	0.081
No Menstrual irregularities	1(4%)	28(17.72%)	
Hyperandrogenism	24(96%)	123(77.85%)	0.034
No hyperandrogenism	1(4%)	35(22.15%)	
Acanthosis Nigricans	20(80%)	9(5.7%)	<0.001
No Acanthosis Nigricans	5(20%)	149(94.3%)	
Increased BMI	22(88%)	95(60.13%)	<0.007
No Increased BMI	3(12%)	63(39.87%)	
Insulin Resistance	21(84%)	4(16%)	<0.001
No Insulin Resistance	48(30.38%)	110(69.62%)	

Discussions- Polycystic ovarian syndrome (PCOS) represents a heterogeneous spectrum of disorders mainly characterized by chronic anovulation/ oligoovulation, clinical or biochemical evidence of hyperandrogenemia or appearance of polycystic ovaries on ultrasonography.[6]It is a disease of adolescent and reproductive age group. In the present study the mean age at presentation was 25.89 ± 4.69 years. Wijayaratne et al[7]found that the mean age for presentation of PCOS in south Asians women was 26 ± 4 years which is consistent with the present study. Similar results also observed by Pierpoint et al[8] & Michaelmore et al.[9]Thyroid abnormality is closely associated with the PCOS patients. We report 25(13.66%) out of 183 PCOS patients had hypothyroidism & 2(1.09%) presented with hyperthyroidism. According to a study conducted by Onno E Janssen et al.[11] hypothyroidism is present in 10.9% of PCOS patient. Another study conducted by Didem Ozdemir et al, reported prevalence of hypothyroidism in 15.9% of PCOS patients[11]. Menstrual problem is one of the commonest symptoms in PCOS patients. We report 158/183(86.34%) patients had menstrual complain. These findings are consistent with a recent Indian study conducted by Aruna et al[12] amongst north Indian women with PCOS, where irregular cycles were present in 80.5% of the patients. In another large series of patients diagnosed with PCOS, 65% to 100% have clinically evident menstrual dysfunction.[13]Menstrual irregularity is associated with women with PCOS with thyroid abnormality. In the present study we did not find any statistical correlations between PCOS with or without hypothyroidism & menstrual irregularity. Some studies shows subclinical hypothyroidism was significantly correlated with disorders of the menstrual cycle in PCOS women[11].The next common symptoms

among married women with PCOS are infertility which may be primary or secondary. In this study, out of 63 married PCOS patients 43(68.25%) were infertile. According to the BMI classification for South Asian population[14] where obesity is BMI ≥25 kg/m2, 117(63.93 %) belonged to obese group. Findings are similar to those obtained in another Indian study conducted by Shringi et al[15] in 2003 where 41.4% of the PCOS patients were overweight. But many studies reports the incidence of obesity could be 50% to 60%,[16] though the incidence may be as high as 80%.[17] There is a statistical significant difference in BMI among patient with or without hypothyroid and PCOS (p=<0.007). A study conducted by Ralf Dittrich et al. in 2008 also confirmed our findings on PCOS with hypothyroid that they are more prone to have increased BMI.[18] PCOS is characterized by hyperandrogenemia and manifest as oligomenorrhoea, acne and hirsutisim. Hirsutism occurs in approximately 70-80% of PCOS patients. We report an incidence of 128(69.94%) in the present study. Similar high incidence of hirsutism was also reported by Azziz et al.[13] and DeUgarte et al.[19] Study by Wijayaratne et al.[2] has found that hirsutism, acne and acanthosis nigricans were significantly more prevalent in South Asians women. Balen et al. had noticed 37% prevalence rates for acne among women with PCOS[20]. Acne is seen in approximately one third of PCOS patients[20,21] and conversely a majority of women with severe or resistant acne have PCOS. We report an incidence of 65(35.52%) of patients had acne. Insulin resistance is one of the basic mechanism which leads to multiple symptoms complex in them. Considering the cut off value of serum fasting insulin for hyperinsulinemia as more than or equal to 20 µIU/ml, the prevalence of hyperinsulinemia among PCOS patients was found to be 69 (37.705%) in this study. Fasting hyperinsulinemia has been used as a measure of insulin action.[22] South Asian PCOS have higher fasting insulin concentrations and lower insulin sensitivity (higher insulin resistance).[2] Fasting plasma glucose to fasting insulin ratio is a good measure of insulin sensitivity in PCOS women and has both high sensitivity and specificity for detecting insulin resistant women. Considering this as the parameter for insulin sensitivity and the cut off as a ratio < 4.5,[22] the prevalence of insulin resistance (IR) was found to be 69(37.705%). Comparable findings were also obtained by Huang et al.[23] in their recent study. However the prevalence as reported by Legro et al.[17] in Hispanic population was 53%. We have found a statistically significant association between hypothyroid and insulin resistance (p=<0.001). According to Ralf Dittrich et al. 50-70% of PCOS patients have insulin resistance and a significant association between thyroid function, as reflected by TSH >2.5 mIU/L and insulin resistance was found in patients with PCOS patients and this association appeared to be independent of age and BMI.[18] Pallotti et al observed a close relationship between insulin secretion, and thyroid and ovarian function in patients suffering from PCOS.[24] The association between them is considered to be extremely statistically significant. In this study, out of 25 cases of PCOS with hypothyroidism, 24(96%) had features of hyperandrogenism like hirsutism and acne. According to a study conducted by Dahiya k et al, serum testosterone levels were found to be increased in PCOS patients with hypothyroidism[4] which leads to increased manifestations of hyperandrogenism like hirsutism and acne. This may be explained as hypothyroidism reduces sex hormone binding globulin and increases free testosterone. In another study conducted by Z Velija-Asmi et al. serum testosterone and its manifestations like hirsutism and acne are more common in PCOS with subclinical hypothyroidism.[11] In this study, 20(80%) of PCOS with hypothyroidism had acanthosis nigricans, and 9(5.7%) out of 158 cases of PCOS without hypothyroidism had acanthosis nigricans (p= 0.001). Study conducted by Trinh Hermanns et al. also reported Acanthosis nigricans, a finding common in patients with PCOS, has been reported to have a positive correlation with hypothyroidism.[25]

Conclusion- PCOS and hypothyroidism are closely related. There is increased prevalence of hypothyroidism in PCOS. The symptoms of both PCOS and hypothyroidism are similar. PCOS patients with hypothyroidism have increased prevalence of menstrual complaints like oligomenorrhea and secondary amenorrhea. PCOS patients with hypothyroidism have increased prevalence of hyperandrogenism , acanthosis nigricans , insulin resistance and increased BMI. As the features of both PCOS and hypothyroidism are overlapping and an association between these two disease states is not uncommon , thyroid profile should be analyzed which may help in better understanding of the etiology and management of PCOS. The relationship between thyroid profile and PCOS is being tried to be explored more and thus the problem of PCOS can be solved to some more extent.

REFERENCES:

1. March WA, Moore VM, Willson KJ et al. The prevalence of PCOS in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544-51.
2. Wijeyaratne CN, Balen AH, Barth JH, Belchetz PE. Clinical manifestations and insulin resistance in polycystic ovary syndrome among south Asians and Caucasians: is there a difference? Clin.Endocrinol.2002; 57:343-50.
3. The Rotterdam ESHRE/ASRM- Revised 2003 Consensus on diagnostic criteria and long term health risks related to PCOS. Hum Reprod. 2004;19:41-47.
4. Dahiya K, Sachdeva A, Singh V, Dahiya P, Singh R, Dhankhar R, Ghalaut P, Malik I. Reproductive hormone and thyroid hormone profile in PCOS. Webmed central Endocrinology 2012;3(6):WMC003455.
5. Harrisons Textbook of internal medicines 19th edition.
6. Katsiki N, Giadou EG, Hatzitolios A. The role of insulin sensitizing agents in the treatment of polycystic ovary syndrome. Drugs 2009;69(11):1417-1431.
7. Chandrika N Wijeyaratne, Ruwanthi de A Senaviratne, Shamalka Dahanayake, Adam H Balan. Phenotype and metabolic profile of south asian women with PCOS. Human Reproduction.2011;26(1):202-213.
8. Pierpoint T, McKeigue P, Issacs A and Jacobs HS. Mortality of women with polycystic ovary syndrome at long term follow up. J Clin Epidemiol.1998;51:581-586.
9. K.F.Michelmore, A.H. Balen and D.B.Dunger. Polycystic ovaries and eating disorders: are they related? Hum. Reprod.2001;16(4):765-769.
10. Lynn L. Amowitz, MD, MSPH, Burton E. Sobel,MD. Cardiovascular consequences of polycystic ovary syndrome. Endocrinology & Metabolism Clinics of North America.1999;28(2):439-458.
11. Z. Velija-Asimi, Sarajevo, Bosnia and Herzegovina. The role of subclinical hypothyroidism and vitamin D deficiency in the development of menstrual disorders in women with PCOS. Endocrine Abstracts .2012;29:916.
12. J. Aruna, S.Mittal, S. Kumar, R.Misra, V.Dadhwal, N.Vimala. Metformin therapy in women with polycystic ovary syndrome. International Journal of Gynecology and Obstetrics.2004;87:237-241.
13. Azziz R, Sanchez LA, Knochenhauer ES et al. Androgen excess in women: experience with over 1000 cocsecutive patients. J Clin Endocrinol Metab.2004; 89:453-462.
14. Chamukuttan Snehalatha, Vijay Viswanathan and Ambady Ramachandran. Cutoff values for normal anthropometric variables in Asian Indian adults. Diabetes Care.2003;26(5):51380-51384.
15. Shringi M, Vaidya RA, Vaidya Ab et al. Insulin resistance in polycystic ovarian syndrome: A study of 90 patients. Indian J Endocrinol Metab 2003;1:19-23.
16. A Gambineri, C Pelusi, V Vicennati, U Pagotto and R Pasquali Obesity and the polycystic ovary syndrome. International journal of obesity.2002;26(7) 883-896.
17. Legro RS, Kunselman AR, Dunaif A. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. Am J Med 2001;111:607-13.
18. Ralf Dittrich, Natia Kajaria, Susanne Cupisti, Inge Hoffmann, Matthias W Beckmann, Andreas Mueller. Association of thyroid stimulating hormone with insulin resistance and androgen parameters in women with PCOS. Human Reproduction, 2008;.24(11):2924-2930.
19. Catherine M DeUgarte, Alfred A. Bartolucci, Ricardo Azziz. Prevalence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. Fertility and sterility 2005;83(5):1454-1460.
20. Balen AH, Konway GS, Kaltsas G et al. Polycystic ovary syndrome: The spectrum of the disorder in 1741 patients. Hum Reprod 2002;17(9):2219-2227.
21. Frank S. Polycystic ovary syndrome: a changing perspective. Clin. Endocrinol.1998; 31:87-118.
22. Kirsten A. McAuley, Sheila M. Williams, Jim I. Mann, Robert J.Walker MD,Nick J. Lewis-Barned, Lara A. Temple, and Ashley W. Duncan, BSC. Diagnosing Insulin resistance in the general population. Diabetes care.2001;24(3):3460-64.
23. Huang J, Ni R, Chen X et al. Metabolic abnormalities in adolescents with polycystic ovary syndrome in south China. Reprod Biol Endocrinol.2010;17(8):142.
24. Pallotti S, Gasbarrone A, Franzese IT. Relationship between insulin secretion, and thyroid and ovary function in patients suffering from polycystic ovary. Minerva Endocrinol 2005;30(3)193-97.
25. Trinh Hermanns-LêAndré ScheenGérald E. Piérard. Acanthosis Nigricans Associated with Insulin Resistance. American Journal of Clinical Dermatology.2004; 5(3):199–203.