Original Article

Association of altered thyroid function and prolactin level in polycystic ovarian syndrome

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Abstract

Polycystic ovarian syndrome (PCOS) is a common disorder for female with fertile age. Along with other clinical and biochemical manifestations, thyroid function and prolactin level may be altered in patients with PCOS. This study aimed to evaluate the clinical and biochemical status, as well as alteration of thyroid stimulating hormone (TSH), prolactin (PRL) level in patients with PCOS. Present study comprised of 100 diagnosed PCOS patients according to revised Rotterdem Consensus criteria. All patients were studied for serum testosterone, LH (lutenizing hormone), FSH (follicle stimulating hormone), blood glucose, lipid profile as well as TSH, FT4 (free thyroxin) and prolactin level. Out of 100 PCOS patients 97 had hirsutism, 64 had acanthosis nigricans, where menstrual irregularities were in 94 patients. Diastolic blood pressure *(74±1.1 vs. 77±0.9, mmHg; p=0.017), total cholesterol (163±5.3 vs. 193±6.2 mg/dl; p<0.001), low density lipoprotein (LDL, 104±3.7 vs. 124±4.9 mg/dl; p=0.002) and frequency of acanthosis (25% vs. 75%; p<0.001) were significantly higher among the patients having BMI>25 Kg/m^2 than those of have ≤ 25 Kg/m^2. Among the fertile women (n=53), 47% had primary and 41.5% had secondary infertility; whereas of the total patients, 21% had altered thyroid function and 6.1% had raised prolactin (PRL, ng/ml) level. Differences of TSH (4.1±3.6 vs. 3.5±6.8, mIU/L; p=0.725) was not significant; whereas level of PRL (13.87±6.9 vs. 9.4±5.2 ng/ml; p=0.018) was significantly higher in the group of primary infertility. Hirsutism, menstrual disturbance and acanthosis were very common in PCOS. Both primary and secondary sterility were also commonly observed and PRL was higher in primary infertility. About one fifth of PCOS had altered thyroid function.*

Keyword: Polycystic Ovary Syndrome, altered thyroid function, prolactin level

Introduction

Polycystic ovarian syndrome (PCOS) is a disorder of premenopausal women characterized by hyperandrogenism and chronic anovulation. The polycystic morphology of the ovary is consistent with, but not essential for the diagnosis of the syndrome.[1] It has significant and diverse clinical implications including reproductive (infertility, hyperandrogenism, hirsutism), metabolic (insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, adverse cardiovascular risk profiles) and psychological features (increased anxiety, depression).[2]

Although there is no universally accepted definition of PCOS, diagnostic criteria as established by the National Institute of Health (NIH) in 1990 are the combination of menstrual disorder together with clinical and/or biochemical hyperandrogenism. The revised criteria by Rotterdam consensus conference, 2003 defined PCOS by the presence of two or more of the followings: clinical and/or biochemical hyperandrogenism, oligomenorrhoea or anovulation and polycystic ovaries after exclusion of other aetiology (congenital adrenal hyperplasia, androgen secreting tumor, Cushing syndrome etc.).[3] The prevalence of PCOS in general population has been estimated to be 5% to 10% of women in reproductive age.[1]

The exact pathophysiology of PCOS is complex and remains largely unclear. During the reproductive years, PCOS is associated with important reproductive morbidity including infertility, irregular uterine bleeding and increased pregnancy loss.[2] It is not uncommon for women with PCOS to either have hypothyroidism in addition to PCOS, or they may have been misdiagnosed with PCOS when they actually have an underactive thyroid gland.[4] Many of the symptoms of hypothyroidism mimic the symptoms of PCOS.

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Thyroid dysfunctions interfere with numerous aspects of reproduction and pregnancy. Several articles have highlighted the association of hyperthyroidism or hypothyroidism with menstrual disturbance, anovulatory cycles, decreased fecundity and increased morbidity during pregnancy.[5] Although the underlying causes of hypothyroidism and PCOS are completely different, these two entities have many features in common, including oligo- or anovulation; decreased serum SHBG; increased serum free testosterone, LH (lutenizing hormone) and cholesterol concentrations.

PCOS and subclinical hypothyroidism both have adverse effect on metabolic parameters separately.[6] In women with PCOS, who frequently have insulin resistance and metabolic syndrome, subclinical hypothyroidism developing in addition may aggravate insulin resistance. Women with PCOS might therefore be candidates for screening in order to identify disturbances in thyroid function.

Prolactin is a polypeptide hormone secreted by the anterior pituitary gland, whose main role is to stimulate lactation in the postpartum period. Hyperprolactinemia induces suppression of the hypothalamic-pituitary-gonadal axis and resistance of the ovary to gonadotropin action, which results in amenorrhea and anovulation. Hyperprolactinemia adversely affects the fertility potential by impairing pulsatile secretion of GnRH and hence interfering with ovulation. Both PCOS and hypothyroidism are commonly associated with hyperprolactinemia and such patients exhibit ovulatory failure. So the present study was conducted to determine the altered thyroid function frequency and prolactin level in diagnosed PCOS patients.

Methods

The study was an observational, cross-sectional one. 100 PCOS patients with the age range of 15-45 years diagnosed on the basis of Rotterdam 2003 criteria were recruited from Endocrine inpatient and outpatient department of BSMMU. All patients fulfilled Rotterdam criteria i.e. had 2 of the following - oligomenorrhoea or anovulation, clinical or/and biochemical sign of hyperandrogen and polycystic ovaries. Exclusion criteria were any serious co morbid condition, suspected CAH, ovarian or adrenal tumor. TSH > 4μIu /ml was termed raised TSH and FT_4 < 0.8ng/dl was termed low FT_4. Serum prolactin > 25ng/ ml was termed Hyperprolactinemia.

Serum Thyroid Stimulating Hormone (TSH) and serum free thyroxin (FT_4) level and serum Prolactin level were the main variables to be studied. Measurement of TSH and prolactin was done by the ADVIA Centaur CP, manufactured by Siemens Healthcare Diagnostic Inc., USA. It is a two site sandwich immunoassay using direct chemiluminescent technology. FT_4 measurement was also done by the ADVIA Centaur CP, manufactured by Siemens Healthcare Diagnostic Inc., USA. It is a competitive immunoassay using direct chemilumin- escent technology.

All data were processed using the SPSS program of version 13.0 and expressed in frequencies or percentages. Mean values were expressed as mean ± SD/SE. Comparison of mean values between groups was done by Student's t-test and discrete values were compared by Chi-Square test.

Results

Mean age of the study subject was 23 ± 7(mean ± SD) in fertile women and the mean BMI was (27 ± 5.18, kg/m^2). Near cent percent had hirsutism (97%) and menstrual irregularities (94%), whereas, acanthosis nigricans were present in 64%. (Table-I)

Table-I: Characteristics of the patients (n=100)

Characteristics	Value (Mean/ Number) (±SD)/(%)
Number of cases	100
Age in years	23 (±7)
Weight in kilogram (kg)	64 (±13)
Height in meter (m)	154 (±6)
BMI in kg/m^2	27 (±5.18)
Hirsutism	97 (97%)
Menstrual irregularities	94 (94%)
Acanthosis Nigricans	64 (64%)
SBP in mmHg	117 (±10)
DBP in mmHg	76 (±7)

On comparison of variables between PCOS patients having normal thyroid function and its aberration, none of the variables i.e. age (year, p= 0.941), height (meter, p= 0.763), weight (kg, p= 0.845), BMI (kg/m^2, 0.740), SBP (mmHg, p= 0.818), diastolic blood pressure (mmHg, p= 0.979), hirsutism (p= 0.511), menstrual irregularities (NS) excepting acanthosis (p= 0.079) varied between the two groups. (Table-II)

Table-II: Comparison of clinical parameters between euthyroid women with PCOS with altered thyroid function

Clinical parameters	Euthyroid (n = 79)	Altered Thyroid Function (n = 21)	p - value
Age (year)	23 ± 4.93	23 ± 3.7	0.941
Height (m)	2 ± 0.06	2 ± 0.07	0.763
Weight (kg)	64 ± 13.8	64 ± 9.4	0.845
BMI (kg/m2)	27 ± 5.4	27 ± 4.2	0.74
SBP (mmHg)	117 ± 10.1	116 ± 10.7	0.818
DBP (mmHg)	76 ± 7.3	76 ± 5.3	0.979
Hirsutism	77 (97.5%)	20 (95.2%)	0.511
Menstrual disturbance	74 (93.7%)	20 (95.2%)	1
Acanthosis	47 (59.5%)	17 (81%)	0.079 *

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure * indicates statistically significant

Hormones concerning to PCOS, blood sugar (both FBS and 2 hours after 75 gm glucose) and lipid profile of the patients having euthyroid status and aberrant thyroid function were compared. No significant difference was observed between the two groups for any variables -LH (mIU/L, *p*= 0.867), FSH (mIU/L, *p*= 0.752), serum testosterone (ng/dl, *p*= 0.192), serum prolactin (ng/ml, 0.580), FBS (mmol/L, *p*= 0.471), 2 hour OGTT (mmol/L, *p*= 0.843), total cholesterol (mg/dl, *p*= 0.178), LDL (mg/dl, *p*= 0.212), HDL (mg/dl, *p*= 0.338) and TG (mg/dl, *p*=0.246). (Table-III)

Table- III: Comparison of biochemical and hormonal parameters among euthyroid PCOS and PCOS with altered thyroid function

Variables	Euthyroid (Mean±SD)	Altered thyroid function (Mean±SD)	*p* - value
LH (mIU/L)	9.64 ± 11.72	10.11 ± 5.37	0.87
FSH (mIU/L)	4.71 ± 2	4.83 ± 1.43	0.75
Testosterone (ng/dl)	79.43 ± 45	95.28 ± 62	0.19
Serum Prolactin (ng/ml)	11.65 ± 12	13.19 ± 7.9	0.58
FBS (mmol/L)	5.2 ± 0.84	5.0 ± 0.62	0.47
2 hour after 75 gm glucose (mmol/L)	7.2 ± 1.5	7.1 ± 1.8	0.84
Total cholesterol (mg/dl)	177 ± 46.79	192 ± 37.76	0.18
LDL (mg/dl)	113 ± 35.37	124 ± 23.15	0.21
HDL (mg/dl)	43 ± 11.48	40 ± 7.02	0.34
Triglyceride (mg/dl)	152 ± 49	168 ± 77.63	0.25

LDL=low density lipoprotein, HDL=high density lipoprotein, FBS = fasting blood sugar, LH=leutinizing hormone, FSH=follicle stimulating hormone, * indicates statistically significant,

Regarding thyroid function, 21 out of 100 (21%) patients of PCOS had altered thyroid function. (Figure-1)

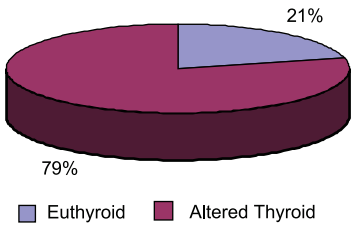

Figure-1: *Altered thyroid function in PCOS*

Among the total study population, 6.1% (6/99) had raised level of prolactin beyond 25ng/ml in this study.(Figure-2)

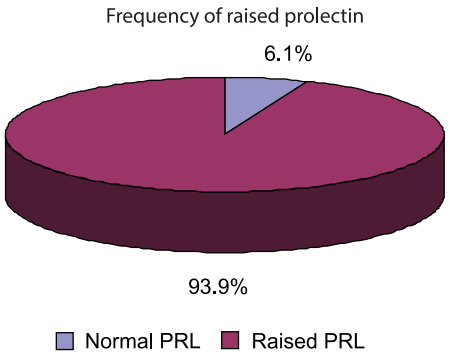

Figure-2: *Prolactin level in PCOS*

Prolactin level differed (ng/ml, 13.87 ± 6.9 vs. 9.4 ± 5.2, *p*=0.018) between the primary and secondary infertility whereas neither TSH (mIU/l, 4.10 ± 3.6 vs. 3.55 ± 6.8, *p*= 0.725) nor FT_4 (ng/dl, 0.182, *p*= 0.018) differed between the primary and secondary infertility. (Table-IV)

Table IV: Relation of infertility with serum TSH, FT_4 and Prolactin level

Infertility	TSH (μIU/ml) (mean±SD)	FT4 (ng/dl) (mean±SD)	Prolactin (ng/dl) (mean±SD)
Primary infertility	4.10 ± 3.6	1.35 ± 0.2	13.87 ± 6.9
Secondary infertility	3.55 ± 6.8	1.43 ± 0.24	9.4 ± 5.2
p-value	0.725	0.182	0.018 *

TSH = thyroid stimulating hormone; FT_4 = free thyroxine * indicates statistically significant

Discussion

Present study was designed to see the alteration of thyroid function, prolactin level and clinical manifestations in PCOS. The study was performed in a tertiary level hospital. A good number of patients had altered thyroid function whereas small number of subjects showed raised PRL level.

PCOS is a complex metabolic, endocrine and reproductive disorder affecting approximately 5-10% of female population in developed countries.[1] Findings from developing countries indicate similar prevalence rates of PCOS.[7] In Bangladesh, there is no population based study for prevalence of PCOS. On the other hand thyroid dysfunction is common in women of reproductive age, with a prevalence of elevated TSH, ranging from 4-9% in this population.[8] Both disorders share some common clinical features like weight gain, irregular cycle, infertility etc. Hyperprolactinemia also causes menstrual disturbance and infertility and not infrequently observed in PCOS.

Prominent clinical manifestations in our study were hirsutism (97%), menstrual irregularities (94%) and acanthosis nigricans (64%). In this study the frequency of raised TSH and PRL are 21% and 6% respectably.

Approximately 50-70% of PCOS patients have been reported to have hyperinsulinemic insulin resistance.[1] These women thus represent a population at high risk for developing metabolic and cardiovascular diseases. When a disturbance of thyroid function occurs in these women additionally, their metabolic and cardiovascular risks may increase dramatically. PCOS and metabolic parameters such as lipids and hormones have been studied in various studies and demonstrated that both PCOS and SCH or hypothyroidism have adverse effect on metabolic parameters separately.[6] But there are a few studies about relationship between thyroid function and alteration in lipids and hormonal levels in women with PCOS.

However, in the present study neither BMI & lipids nor the important clinical manifestations of PCOS or hormones as LH, FSH and testosterone level varied between groups of patients with normal and altered thyroid function. Though some patients (21%) in the present study had altered thyroid function, PRL level was not significantly raised in these patients than that of euthyroid ones. However, PRL level was significantly higher in primary infertility than secondary among married women of fertile age.

Janssen et al, 2004 showed that women with PCOS have a high prevalence of increased TSH.[9] Ganie et al 2011 showed a higher prevalence of the PCOS phenotype in euthyroid adolescent girls with juvenile autoimmune thyroiditis, suggesting a possible role in the pathogenesis of the PCOS phenotype.[10]

In the present study the frequency of raised TSH in PCOS were very few. We selected the PCOS patient from tertiary level hospital. Therefore, it is logical not to extrapolate these data to populations in order to avoid selection bias. It is noteworthy to mention that the study has been a hospital-based one and control group was not included in the study. For a better calculation of intended prevalence of various abnormalities and derangements in PCOS, a population-based study should be conducted in future.

In conclusion, a good number of PCOS patients may have altered thyroid function. From the present study it may be apprehended that thyroid dysfunction and raised prolactin level may be attributable for anovulation and infertility. Without investigations in a large scale, it is difficult to consolidate and precise this suspicion. Therefore, it is proposed that study at large scale might explore the exact link of thyroid dysfunction and prolactin level in PCOS.

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