

Original Research Article

Evaluation of Thyroid Hormones Level in Sudanese Women with Polycystic Ovarian Syndrome

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Abstract: Polycystic ovary syndrome (PCOS) is commonly associated with endocrine, metabolic, cardiovascular and other morbidities. However its association with autoimmune diseases is still controversial. The aim of this study was to evaluate the levels of thyroid hormones and it's antibodies in women with PCOS in Sudan. The method was Ninety female patients with PCOS based on Rotterdam criteria. Together with ninety healthy volunteer females included as controls. Serum levels of Thyroid Stimulating Hormone (TSH), Free Thyroxine (Free T₄), Free Triiodothyronine (Free T₃) and anti-thyro peroxidase antibody (anti-TPO Ab) were tested in the two groups. In results a significant increase was found in TSH and anti-TPO Ab (P<0.05) along with a significant decrease in free T₃ and free T₄ in PCOS females matched against controls (P<0.05). The data suggest that hypothyroidism related to PCOS, and this hypothyroidism could result in auto immune disease. More studies should be carried to reveal the precise relationship of hypothyroidism in the context of PCOS.

Keywords: Thyroid hormones, polycystic ovarian syndrome, anti-thyro peroxidase antibody, autoimmune disease.

INTRODUCTION:

Polycystic ovarian syndrome (PCOS) is the most common form of chronic an ovulation associated with androgen excess; perhaps occurring in 5-10% of reproductive women[1] The clinical manifestation of PCOS includes oligomenorrhea, infertility, acne, hirsutism, fat, and acanthosisnigricans and so on. In addition, these patients may develop with many other related endocrine and metabolic diseases, and have increased risk of suffering endometrial cancer, impaired glucose tolerance, diabetes, and cardiovascular disease [2, 3, 4].

Researches about the pathogenesis of PCOS mainly focus on two interrelated metabolic elements-insulin resistance (IR) and hyper androgenism. Nevertheless, pathogenesis of PCOS still remains unclear.[5] Thyroid gland dysfunction leading to hypothyroidism is a common disorder affecting women more often than men. The clinical features of hypothyroidism also include weight gain, menstrual irregularities and infertility.[6] An association has been reported between PCOS and hypothyroidism. Most of the times hypothyroidism is subclinical and diagnosed first time during evaluation of PCOS.[7], [8] Triiodothyronine (T₃) and thyroxine (T₄) circulate in blood bound to carrier proteins which are T₄ binding

globulin (TBG), T₄ binding prealbumin (TBPA) and albumin. Approximately 99.97% of T₄ and 99.7 % of T₃ is in bound form and only a small fraction of these hormones circulate unbound and is free for biological activity.[9] Thus, to reach the actual diagnosis and to assess the thyroid function, free fraction of these hormones is essential. Therefore, this study was planned to estimate total and free T₃, free T₄ and thyroid stimulating hormone (TSH) in patients of PCOS.

MATERIAL AND METHOD:

This was a case-control study conducted in Advanced Diagnostic Center, Khartoum state, Sudan; between July 2015 and January 2016. The study included 90 female patients suffering from PCOS.

Diagnosis of PCOS was made according to the Rotterdam European Society for Human reproduction and Embryology/American Society for Reproductive Medicine-sponsored PCOS Consensus Workshop Group.[10]

The protocol was approved by the local ethics committee. All patients gave a written consent. The control group (n=90) consisted of healthy patients who were admitted to check-up unit without any systemic disorder. All women in the control group had regular

menstrual cycle, every 21–35 days. None of the women in the control group had polycystic ovary on ultrasound.

Those participants who had a diabetes mellitus, hyperprolactinemia, congenital adrenal hyperplasia, androgen-secreting tumors, and thyroid disorders including thyroid parenchyma heterogeneity and/or nodular disease on ultrasound and/or thyroid function abnormalities, Cushing syndrome, infection diseases, hypertension, hepatic or renal dysfunction were excluded from the study. The participants under the age of 17 and over the age of 39 were excluded from the study. The participants were also excluded if they had used confounding medications, including oral contraceptive agents, antilipidemic drugs, hypertensive medications, and insulin-sensitizing drugs, within 3 months before enrolment.

All data was analyzed using the Statistical Package for Social Sciences (SPSS) software computer program version 20.0 (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation (SD) following analyzes using independent t-test, which was performed for comparison between control and patient groups. A value of P < 0.05 was considered significant.

RESULT

The data presented in table 1 showed that serum level of TSH and anti-TPO Ab in women with PCOS were significantly elevated compared to healthy control group, while significantly decreased in the serum level of free T₄ and free T₃.

Table 1: Comparison of the means of serum levels of TSH, Free T3, Free T4 and anti-TPO Ab between patient group and control group

Variable	Patients n=90	Control n=90	P.value
TSH	8.4±8.2	1.8±1.3	0.00
Free T3	0.4±0.2	1.0±0.3	0.00
Free T4	5.2±1.9	9.3±2.0	0.00
Anti TPO-Ab	11.6±6.8	3.0±2.1	0.00

The table shows the mean ± SD and probability (P).*

T-test was used for comparison.*

*P.value<0.05 is considered significant.

There was a significant positive correlation found between TSH and anti-TPO Ab (Figure 1), while a significant negative correlation between TSH and free

T₃ (Figure 2) , also a significant negative correlation between TSH and free T₄ (Figure 3) in women with PCOS.

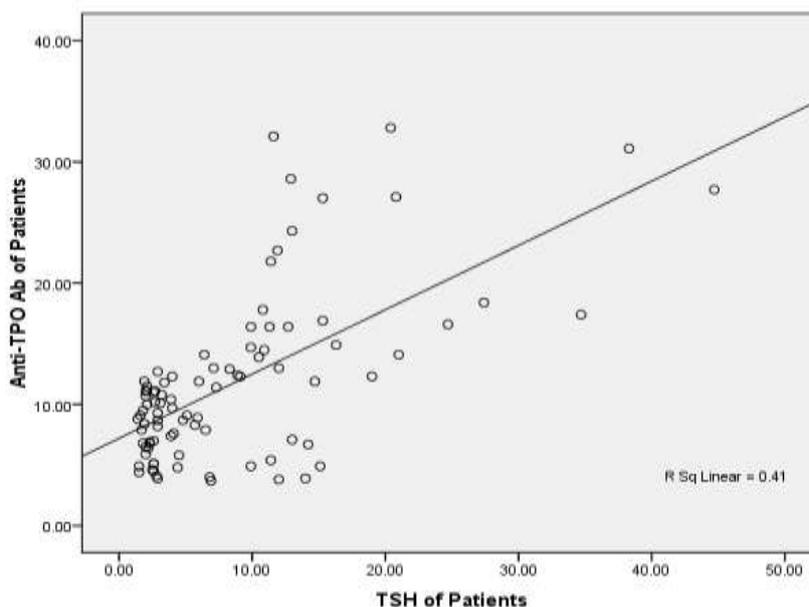


Fig-1: the relation between TSH and anti-TPO Ab in PCOS patients.

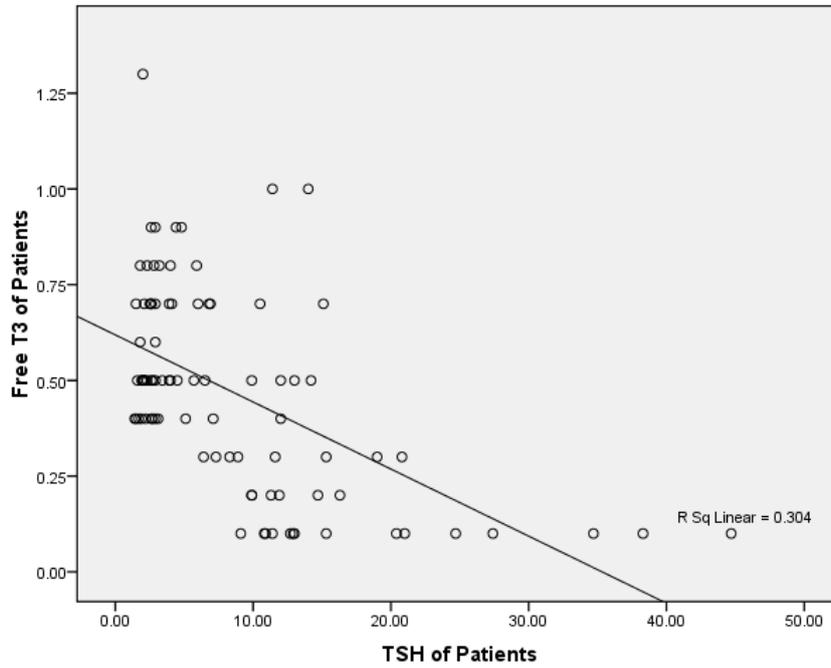


Fig-2: the relation between TSH and free T₃ in PCOS patients.

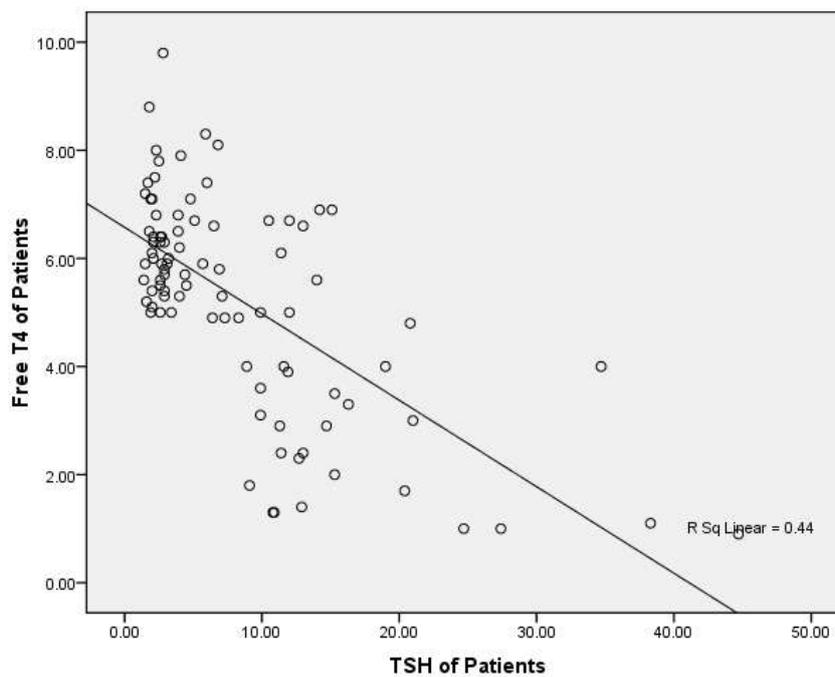


Fig-3: the relation between TSH and free T₄ in PCOS patients.

DISCUSSION

Polycystic ovary syndrome (PCOS), a common endocrinopathy of women of reproductive age, is associated with the early appearance of multiple risk factors for cardiovascular disease, such as abdominal obesity.[11] The present study revealed significantly high TSH level in PCOS patients in contrast to controls ($p < 0.05$). Based on Garber *et al.*; [12], this indicates

the diagnosis of hypothyroidism in PCOS patients. This outcome was in keeping with Janssen *et al.*; [7] who documented a high mean level of TSH in PCOS patients. Besides this, hypothyroidism could be the reason behind PCOS in those patients. Muderris *et al.*; [13] stated that severe prolonged hypothyroidism contributes to bigger ovarian size and/or cyst formation, and additionally, restoration in serum hormone levels

owing to accomplishment of euthyroidism, induces a reduction in ovarian size, resolve of ovarian cysts together with reversal of the polycystic ovary syndrome-like characteristics. At the same time, the study was consistent with Ghosh *et al.*; [14] who, in intending to analyze the part of hypothyroidism in the causation of PCOS, proposed that hypothyroidism resulted in reducing of sex hormone binding globulin level and increment of testosterone level.

In another part of this study we demonstrated similar plasma levels of TSH and also significantly higher prevalence of anti-TPO positivity in patients compared to controls. The overall prevalence of auto immune thyroiditis (AIT) was slightly but not significantly higher in PCOS women. Previous data on the association between PCOS and AIT are controversial. Some reports documented higher prevalence of AIT and higher levels of TSH in PCOS women. Although we found 13% prevalence of hypothyroidism in apparently healthy women, some data suggest that up to 18% of the general population might suffer from hypothyroidism. In a Chinese population of PCOS women higher levels of TSH were documented only in women with a LH/FSH ratio over 3 [15]. Janssen *et al.* presented significantly higher prevalence of anti-TPO antibody in PCOS patients, higher prevalence of AIT and also higher levels of TSH in PCOS women[7]. Comparably, significantly higher titers of anti-TPO antibodies and a higher prevalence of goiter with AIT characteristics were shown in 78 PCOS Iranian women compared to a healthy population[16]. In contrast, a higher prevalence of PCOS in euthyroid girls with AIT has been demonstrated in a previous study[17]. These data suggest a possible role of autoimmunity in the etiopathogenesis of PCOS but this hypothesis is unproven as a recent study clearly documented that PCOS alone was not associated with thyroid disease and the metabolic syndrome or its components appear to be related to thyroid volume, function and antithyroid antibody levels[18].

Concurrently, the present study revealed a significantly lower free T₃ and free T₄ level in PCOS patients as compared to controls (P < 0.05). However, Janssen *et al.*; [7] identified normal thyroid hormone levels in subjects with PCOS. As outlined by Carvalho *et al.*; and Schussler [19, 20] alterations in transporter proteins give rise to altered levels of total T₄ and T₃ irrespective of thyroid status. Based on this consideration, this low free T₄ and free T₃ cannot be explained by isolated thyroid abnormality.

Finally an autoimmune mechanism of PCOS has been suggested by some authors. According to Gleicher *et al.*; this disease might be an opposite condition to premature ovarian failure[21]. Suh *et al.* reported histological findings in a case of PCOS

consistent with autoimmune oophoritis[22] and Lee *et al.*; described a case of a patient with combined PCOS and autoimmune polyglandular syndrome type 2 [23]. Recently Chapman described a fundamental role of thymus and T cells in estrogen induced follicle cyst formation[24]. However studies of anti-ovarian antibodies performed so far have yielded conflicting results. The group of Lonsdale demonstrated ovarian antibodies, and lymphocytic infiltration of ovaries in two patients with PCOS [25]. Some others showed antibodies to human ovarian sections and granulosa cells in patients with PCOS [26-27]. Many other targeting antigens of ovarian immune pathology have been described in PCOS women[28]. In another study, positive anti-ovarian antibodies for at least one isotype were present in 44% of the PCOS women[29] However these results could not be confirmed by others. Nevertheless this aspect of PCOS pathogenesis is still open for further research and requires further studies of other antibodies against various ovarian structures.

In conclusion, the data suggest that hypothyroidism related to PCOS, and this hypothyroidism could result in auto immune disease. More studies should be carried to reveal the precise relationship of hypothyroidism in the context of PCOS.

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