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THYROID FUNCTION AND OTHER METABOLIC CHANGES IN MARRIED AND UNMARRIED FEMALES WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT
It has been reported that there are significant differences in some biochemical markers of PCOS between married and unmarried women with this disorder. The present study was designed to evaluate the correlation of marital status with thyroid hormones, carbohydrate and lipid metabolism, and androgenic activities. Twenty four married and unmarried women with PCOS were evaluated concerning TSH, T3, T4, glycemic control, C-peptide and lipid profile were evaluated in fasting blood samples. The results showed that in both unmarried and married women with PCOS TSH, FPS, C-peptide, and triglycerides levels were significantly elevated compared to healthy control group. Although serum level of TSH was slightly elevated in married women compared to unmarried group, no significant differences were observed in this respect; the same thing was reported for FPS, serum levels of C-peptide and triglycerides, where those parameters shown to be slightly higher in unmarried women but not significantly different from those reported in married group of PCOS women. In conclusion, no correlations were reported for the marital status with thyroid hormones, carbohydrate and lipid metabolism in Iraqi females with PCOS.
KEY WORDS: PCOS, marital status, metabolic changes, thyroid function

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex and heterogeneous disorder affecting 5-10% of women of reproductive age[1,2]. Morbidity of PCOS may include hyperinsulinemia, insulin resistance, early onset of type 2 diabetes mellitus and dyslipidemia[3]. The direct cause of PCOS remain unknown; however, both environmental and genetic factors are implicated, aggregate evidence suggest hypothalamic-pituitary axis (HPA) defects, insulin resistance in skeletal muscles and hypersensitivity of adrenal and ovary tissue to insulin[4,5,6]. The hyperinsulinimic state, present in most women with PCOS, appears to play a central role in development of PCOS and is considered to be the cause rather than the consequence of hyperandrogenism[7], while insulin resistance plays significant role as both a cause and consequence of the syndrome[8]. It has been reported that one of the most other consequences is the development of subclinical hypothyroidism (SCH), which is characterized by elevated serum levels of thyroid-stimulating hormone (TSH) with normal thyroid hormones levels[9]. SCH is considered as an important risk factor for the development of many clinical cardiovascular and endocrine disorders[10], where glucose uptake was impaired in muscles with consequent elevation of plasma insulin[11]. Recently, we reported that there are significant differences in some biochemical markers of PCOS between married and unmarried women with this disorder[12].

Aim of the study

The present study was designed to evaluate the correlation of marital status with thyroid function, carbohydrate and lipid metabolism, and androgenic activities in Iraqi women with PCOS.

PATIENTS AND METHODS

Twenty four women (12 married and 12 unmarried) with an age range of 26.6±4.8 years, body mass index (BMI) of 29.9±1.3 and 30.9±1.6 respectively, previously diagnosed with polycystic ovary and not maintained on any type of therapy were included in the study; the diagnosis of PCOS was based on the classic criteria of hyperandrogenism and chronic anovulation[13]. Twelve healthy women (6 married and 6 unmarried) with age range matched with those of PCOS patients were included and served as control, they have no signs of hirsutism or symptoms of andogenization and all show normal ovulatory menstrual cycles; no significant differences in the studied parameters were reported among them. The study was conducted in the Specialized Center for Diabetes and Endocrinology, Al-Rusafa, Baghdad during the period from July to December 2007. The study protocol was approved by the local committee for clinical study ethics, and informed consent was signed by all participants. Subjects on contraceptive pills or any other hormonal medications were excluded from the study. After an over night fasting, blood samples (10 ml) were drawn from all participants; after preparation of serum, the levels of TSH[14], triiodothyronine (T3)[15], and thyroxine (T4)[16] were analyzed using ELIZA methods according to standard procedures. The levels of glucose[17], cholesterol[18] and triglycerides[19] were analyzed using enzymatic colorimetric methods, while C-peptide level was analyzed utilizing immunoradiometric assay (IRMA) method. All results were expressed as mean ± SEM, and statistically analyzed utilizing Analysis of Variance (ANOVA) for comparison. Post-hoc test was carried out with log transformation; values with P values less than 0.05 are considered significantly different.

RESULTS

The data presented in table 1 showed that in both unmarried and married women with PCOS TSH, FPS, C-peptide, and triglycerides levels were significantly elevated compared to healthy control group; while other studied parameters did not show any significant differences. Evaluation of data of both patients groups revealed that although serum level of TSH was slightly elevated in married women compared to unmarried group, no significant differences were observed in this respect; the same thing was reported for FPS, serum levels of C-peptide and triglycerides, where those parameters shown to be slightly higher in unmarried women but not significantly different from those reported in married group of PCOS women (Table 1).

DISCUSSION

The data presented in table 1 demonstrate that presence of insulin resistance in both groups of PCOS women and this was associated with sub-clinical hypothyroidism, as revealed by normal T3 and T4 levels and elevation in serum TSH levels; this finding was consistent with many recent studies in this respect[20,21]. However, the reported

insulin resistance does not seem to be clinically relevant in terms of significant hyperglycemia, but as a result of decrease in hepatic glucose output as a consequence of hyperinsulinemia[22]. The existence of a relationship between thyroid function and possibility of alteration in lipid profile and other metabolic parameters is very well addressed[23]. In the present study, there is a significant increase in TSH level in both groups of PCOS patients, which is associated only with impaired TG serum levels; this may attributed to that the increase in TSH levels only is not enough to predispose to impaired all lipid profile components. Moreover, PCOS is found to be associated with life time risk of dyslipidemia[24], and different pattern of dyslipidemias can be reported both in lean and obese PCOS[25], with consequent elevation of TG and decrease in HDL-c levels, and elevation of TG/HDL-c ratio is associated with insulin resistance in general population. Cataldo et al. have shown that fasting TG/HDL ratio, when elevated to about 1.5, may be useful to support the diagnosis of insulin resistance in women with PCOS[26], and those with higher serum TSH and relative insulin resistance are at greatest risk of dyslipidemia[23]. In the present study, the elevation in FPG and C-peptide levels can be interpreted on the bases that thyroid function is associated with glucose metabolism; during hypothyroidism, glucose uptake in muscles and adipose tissues is found resistant to the influence of insulin resulting in higher concentration of insulin in the plasma of PCOS patients[11] and approximately 50-70% of them has been reported to have hyperinsulinemia and insulin resistance[27]. Women with reported sub-clinical hypothyroidism have significantly higher body mass index (BMI), which is also known to influence thyroid hormone concentrations, with higher TSH levels in obese women[28]; the patients included in the present study markedly showed such pattern of BMI changes that support the previously reported data in this respect. Many studies in human and other mammalian species have yield evidence that adipocytes and preadipocytes possess thyrotropin receptors[29,30,31]. Many *in vitro* and *in vivo* studies demonstrated that the action of thyrotropin via its receptors in fat tissues induces differentiation of pre-adipocytes into adipocytes and expansion of adipose tissue volume (adipogenesis)[32,33]. Adipose tissue is considered as a major endocrine gland, producing and releasing numerous adipokines, which have metabolic and/or inflammatory effects in other tissues, including the liver, muscles, pancreatic β-cells and the brain[34]. It has been reported that, in obese diabetic rodents, treatment with thyroid hormone enhances insulin sensitivity and reduce hyperglycemia and hyperinsulinemia; thyroid hormone also cooperate with catecholamines to enhance lipolysis and reduce visceral fat mass, with consequent improvement in insulin resistance[35]. On the other hand, higher circulating levels of insulin may increase proliferation of thyroid tissue[36], where evidence showed that insulin receptors are over-expressed in most thyroid tumors as an early step in thyroid carcinogenesis[37]. There is also an association between disturbed thyroid function and ovarian function, infertility, early pregnancy loss and morbidity during pregnancy[38]. An alteration in insulin resistance indices was observed in women with PCOS associated with sub-clinical hypothyroidism in comparison with PCOS women with TSH<2.5 mIU/L, which appeared to be associated with TSH concentrations [39]. In conclusion, no correlations were reported for the marital status with thyroid hormones, carbohydrate and lipid metabolism in Iraqi females with PCOS.

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Table 1. Serum levels of TSH, T_3, T_4, glucose, C-peptide cholesterol, and triglycerides in married and unmarried women with PCOS

Parameters	**Control n= 12**	**Unmarried with PCOS n= 12**	**Married with PCOS n= 12**
TSH mIU/L	3.23 ± 0.23^a	5.98 ± 0.66^b	6.48 ± 0.66^b
T_3 ng/dL	128.9 ± 5.4^a	124.9 ± 7.2^a	129.2 ± 0.2^a
T_4 µg/dL	7.8 ± 0.49^a	7.8 ± 0.42^a	7.2 ± 0.43^a
glucose mmol/L	4.7 ± 0.16^a	5.7 ± 0.39^b	5.02 ± 0.23^b
C-petide ng/ml	4.05 ± 0.28^a	6.94 ± 0.58^b	6.66 ± 0.8^b
Cholesterol mmol/L	4.73 ± 0.14^a	4.73 ± 0.14^a	5.28 ± 0.32^a
Triglycerides mmol/L	1.52 ± 0.08^a	2.37 ± 0.29^b	2.23 ± 0.2^b

Data presented as Mean±SEM; n= number of subjects; values with non-identical superscripts (a,b) within the same parameter are significantly different (P<0.05)

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