ORIGINAL ARTICLE

The relationship of serum 25-dihydroxy vitamin D3 concentrations with metabolic parameters in non-obese women with polycystic ovarian syndrome

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Abstract *Introduction:* Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age, which is associated with an increased risk of developing metabolic syndrome (MBS). Recently, many studies have started to dig up the dramatic effect of vitamin D deficiency on PCOS patients suffering from the MBS. However, little is known about the role of this fat-soluble agent in non-obese PCOS women. *Aim:* To investigate the relationship between serum 25-dihydroxy vitamin D3 [25(OH) D] levels and metabolic parameters in non-obese women with PCOS. *Materials and methods:* Eighty-eight non-obese women who underwent PCOS were experimentally evaluated. Patients were divided into two categories according to their body mass index (BMI): patients with normal weight and overweight patients. The serum levels of 25(OH) D, FBS, CRP, TC, TG, LDL, HDL, insulin as well as the insulin resistance indexes were assessed in all the study patients. *Results:* The mean age of the patients was 27 years, 36 (40.9%) had normal weight and 52 (59.1%) were overweight. Vitamin D deficiency was observed in 84.1% of the patients, but its variations between both groups were not significantly different. A significant correlation was found between 25(OH) D levels and the patients' age, as well as the HDL serum concentration. Furthermore, there was no significant association between 25(OH) D levels

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and insulin resistance index in both groups with PCOS. *Conclusion:* Our study found no association between lower 25(OH) D levels and increased risk of metabolic disturbances and insulin resistance in non-obese patients with PCOS.

1. Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age. Its worldwide prevalence has been estimated between 2.2% and 26%, which is reported about 7.1% among Iranian population (1). These patients generally are more likely have irregular menstruation, hyperandrogenism, and defects in ovulation and polycystic ovaries (2). Although several diagnostic criteria have been reported for PCOS, Rotterdam is known to be the most important prognostic factor in such patients. Based on this criteria, the diagnosis was made with the presence of at least two of the following features: irregular or failed ovulation, clinical symptoms and laboratory findings of hyperandrogenism or the presence of polycystic ovarian morphology confirmed by ultrasonography (3).

PCOS women have an increased risk of developing metabolic syndrome (MBS), as they show up two times higher prevalence of this disorder compared to normal population (4). Insulin resistance, obesity, impaired glucose metabolism, dyslipidemia and hypertension are the main characteristics of MBS. It has also been shown that the insulin resistance has a pivotal role in the pathogenesis of PCOS and MBS (5), so 50–80% of PCOS patients suffer from insulin resistance syndrome (6). Hypoglycemia is one of the most common complications of insulin resistance, which in turn can lead to hyperinsulinemia, enhanced LH hormone action and elevated androgen levels, in the following. Thus, a sequence of point events should be classified as underlying causes of PCOS (7). More recently, it has been demonstrated that vitamin D deficiency is associated with insulin resistance and particularly affects the amount of insulin, released from pancreatic beta cells (8). However, the prevalence of vitamin D deficiency is a common finding in PCOS women, as approximately 67–85% have a serum 25(OH) D concentration of less than 20 ng/ml. Ovulation problems, menstrual irregularities and infertility are subsequent challenges encountered during the periods of low vitamin D status (9).

Obesity is one of the fastest growing health concerns worldwide. This medical condition, with an impact on hormonal activity and ovulation, represents one of the most important risk factors and also a predictor for progression of PCOS (10). Results of several studies have brought important evidence linking obesity with vitamin D deficiency (11). Therefore, current findings have raised the question of whether obesity and vitamin D deficiency might have different levels of efficacy in the development of PCOS among susceptible subjects. The purpose of this study was to determine the effect of serum 25(OH) D concentration on metabolic parameters and insulin resistance in non-obese patients with PCOS.

2. Materials and methods

This experimental study was performed on 88 non-obese women with PCOS, ranging in age from 19 to 40 years. We used Rotterdam criteria for the diagnosis of PCOS, including menstrual problems such as oligomenorrhea (fewer than 6 periods per year) or amenorrhea (the absence of menstrual periods for more than 6 months), clinical symptoms and laboratory findings of hyperandrogenism in addition to sonographic evaluation of PCOS (the presence of > 12 follicles measuring 2–9 mm in diameter or an ovarian volume more than 10 cm^3) (3). Patients with nonclassic congenital adrenal hyperplasia, thyroid disorders, androgen-secreting tumors, Cushing's syndrome and hyperprolactinemia, as well as cases with a history of drug use within the past three months, affecting calcium and carbohydrate metabolisms and endocrine parameters, are excluded from the study. Our research was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences and all the patients signed an informed consent before entering the study. Body mass index (BMI) was calculated from adjusted weight and height, with unit kg/m^2. The population selected was then divided into two groups: normal weight (BMI $\leqslant$ 25 kg/m^2) and overweight (BMI > 25 kg/m^2).

Fasting venous blood samples were collected during the follicular phase of the menstrual cycle (between the 3rd and 5th day of menses) and serum was separated, stored at −20 °C until they were transported for analysis of biochemical factors. Serum concentrations of 25(OH) D by radioimmunoassay (DRG, Marburg, Germany), insulin by IRMA assay (Bio-Source Europe S.A. Nivelles, Belgium), as well as high-sensitivity C-reactive protein (hs-CRP) by Architect c16000 (Abbot) system were measured for all the patients with PCOS. Serum glucose, triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were also obtained by standard methods (CinnaGen, Tehran, Iran). The insulin resistance index was calculated by homeostasis model assessment (HOMA) as follows (12):

$$[\text{Fasting Insulin (mIU/mL)} \times \text{Fasting Glucose (mg/L)}]/405$$

Statistical analyses were performed using SPSS 16.0. The difference in mean levels of metabolic factors between normal weight and overweight PCOS subjects was determined by and independent *t*-test. The Pearson Correlation test was then done to evaluate the relationship between BMI index and metabolic dysfunction. Results were considered significant with a *P*-value of less than 0.05.

3. Results

Patients' age ranged from 19 to 40, with a mean age of 27 years. Of these, 36 (40.9%) had a normal BMI of