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Association between Vitamin-D with Metabolic Parameters in Polycystic Ovarian Syndrome.

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ABSTRACT

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder that affects women of reproductive age leading to metabolic alterations such as hyperandrogenism, obesity, menstrual irregularities, insulin resistance, and polycystic ovaries. In the present study, association between vitamin-D with metabolic parameters in polycystic ovarian syndrome in the Indian population was studied. The study population included 125 participants with 65 patients diagnosed for PCOS and 60 normal age matched controls. The participants in the study were included after their informed and written consent. The glucose, insulin, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides and vitamin D levels were estimated. IR was estimated using the homeostatic model assessment-IR (HOMA-IR). The FBS, insulin and HOMA-IR showed significantly high in PCOS patients when compared with the control subjects. High Density Lipoprotein was significantly less in PCOS patient, Low-Density Lipoprotein was significantly high in PCOS patients, but total cholesterol, triglyceride and HDL/ LDL ratio did not show any significant variation between case and controls. Polycystic ovary syndrome cause endocrine and metabolic imbalance, causing irregular menstrual cycles, dyslipidemia, and infertility.

Keywords: PCOS, Lipid Profile, HOMA-IR

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder that affects women of reproductive age leading to metabolic alterations such as hyperandrogenism, obesity, menstrual irregularities, insulin resistance, and polycystic ovaries. (1). The etiology remains unclear, but several genetic and environmental factors have been correlated with manifestations of this syndrome (2). Several pathways have been implicated in the etiology of PCOS. These include the metabolic or regulatory pathways of steroid hormone synthesis, regulatory pathways of gonadotropins action, the insulin-signaling pathway, and pathways regulating body weight. Several genes from these pathways have been tested as candidate genes for PCOS (3).

Vitamin D level plays important roles in metabolic pathways affected by PCOS, including calcium homeostasis, the insulin pathway, polymorphisms have been shown in some studies to have an association with some of the patterns presented by PCOS(4). Vitamin D is one of the key regulating hormones in calcium homeostasis. It has been shown that calcium plays a role in oocyte activation and maturation resulting in the progression of follicular development (5).

It has been speculated that most individuals in India are deficient in Vitamin D and its deficiency has become an epidemic in our country. There is widespread prevalence of varying degrees of Vitamin D deficiency with low dietary calcium intake in Indian population according to various studies published earlier [6,7]. A deficiency of Vitamin D not only causes poor bone mineralization but also has been implicated in numerous chronic diseases. Vitamin D deficiency is common in women with polycystic ovary syndrome (PCOS). Vitamin D deficiency may intensify symptoms of PCOS, with observational studies showing lower 25(OH)D levels were associated with insulin resistance, ovulatory and menstrual irregularities, lower pregnancy success rate, hirsutism, hyperandrogenism, obesity and elevated cardiovascular disease risk factors [8].

It has been reported that vitamin D deficiency reduces mating success and fertility in female rats. Female rats fed a vitamin D deficient diet are capable of reproduction, but overall fertility is decreased by 75%, and litter size is reduced by 10% [9]. Both VDR and 1α-hydroxylase knockout female mice are infertile and present with uterine hypoplasia, impaired folliculogenesis, and an ovulation [10-12]. In the present study, association between vitamin-D with demographic and metabolic parameters in polycystic ovarian syndrome in the Indian population was studied.

MATERIALS AND METHODS

The present case control study was conducted in the department of Obstetrics and Gynecology at K.S. Hedge Charitable Hospital, Deralakatte, Mangalore and biochemical estimations were performed at Central Research Laboratory of the institute. The study population included 125 participants with 65 patients diagnosed for PCOS and 60 normal age matched controls. The participants in the study were included after their informed and written consent. The study protocol was approved by the institutional ethics committee and the approval was obtained before the starting of the project.

The women with PCOS, aged between 18-40 years were recruited based on the Rotterdam criteria. Patients clinically diagnosed for hyperandrogenism, such as hyper prolactinemia, androgen secreting tumors, Cushing's syndrome, and non-classical congenital adrenal hyperplasia, and patients on vitamin D or calcium supplementation were excluded. Patients on drugs that alter the sex hormone level like supplementation of Estrogen, Progesterone, combined oral contraceptive pills (OCPs), Gonadotropins and AED drugs were also excluded.

Sixty healthy women between aged 18-40 years with regular menstrual cycles (26–34 days) and normal ovarian morphology were included as controls and pregnant women and subjects not willing to give consent were excluded.

Clinical and biochemical measurements

On the first OPD visit, a detailed history was taken including the age, presenting complaints with duration, detailed menstrual history, past medical and family history. Blood samples for metabolic parameters (glucose, insulin, total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein

cholesterol, and triglycerides (TG)) determinations were collected at 0800–0900 h after overnight fast. IR was estimated using the homeostatic model assessment-IR (HOMA-IR). HOMA-IR was calculated as the product of the fasting plasma insulin value (mU/ml) and the fasting plasma glucose value (mg/dl) divided by 405 (15).For assessing Vitamin D levels, 3 ml of venous blood was collected and centrifuged and serum was stored at -20 degrees until further analysis was performed. Insulin was measured by ELISA (Siemens, Erlangen, Germany) with intra- and interassay CV of 4.0 and 2.6 and 5.1 and 8.4% respectively. 25(OH)D was measured using a commercially available enzyme immunoassay (IDS, Boldon, UK) with intra- andinterassay coefficients of variation (CV) of 5.6 and 6.4%respectively.

Statistical Analysis

Student t test will be used to compare the quantitative data. Association between the categorical variables Chi-Square test was used. P<0.05 was used as statistically significant. Statistical analysis was performed using SPSS version18.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

In the study a total of 125 participants with 65 patients diagnosed for PCOS and 60 normal age matched controls were included.

The summary statistics of different parameters of study subjects were shown in table 1. The fasting blood sugar, insulin and HOMA-IR showed significantly high (p=0.0001) in PCOS patients when compared with the control subjects. Whereas vitamin-D level did not show any significant difference. High Density Lipoprotein was significantly less in PCOS patient. Total cholesterol (p=0.724), triglyceride (p=0.106) and HDL/ LDL ratio (p=0.053) did not show any significant variation between case and controls (figure-1).

The association between metabolic parameters of study subjects was shown in table 2. There was no significant association between the vitamin D level and metabolic parameters studied between the case and control except Insulin which shows a significant association ($\chi2$= 6.2634, p=0.012).

Table 1: Summary statistics of different parameters of study subjects. Values are expressed as Mean ± SD.

PARAMETER	CASE(n=65)	CONTROL(n=60)	P value
FBS (mg/dl)	85.90±18.21	67.93±8.08	0.0001**
INSULIN (µIU/mL)	18.32±17.69	5.12±9.88	0.0001**
HOMA-IR	6.28±1.2	2.4±0.1	0.0001**
VITAMIN D(ng/ml)	22.56±7.00	25.61±8.69	0.721, NS

Note: **=highly significant, NS=Non significant

Table 2: Summary statistics of showing the association between metabolic parameters of study subjects. Values are expressed as Mean ± SD.

PARAMETERS	CASE(n=65)	CONTROL(n=60)	χ2 Value	p- Value
FBS	85.90±18.21	67.93±8.08	$\chi2$= 1.2025	p= 0.272, NS
Insulin	18.32±17.69	5.12±9.88	$\chi2$=6.2634	p=0.012*
HOMA-IR	6.28±1.2	2.4±0.1	$\chi2$=2.1668	p=0.141, NS
TG	107.9±38.43	97.91±28.52	$\chi2$=0.4773	p=0.489, NS
TC	159.46±37.21	157.36±28.29	$\chi2$= 0.1936	p=0.659, NS
HDL	53.12±9.12	66.66±11.45	$\chi2$=0.108	p=0.742, NS
LDL	97.12±38.28	75.18±25.08	$\chi2$=1.3743	p=0.241, NS
LDL/HDL	1.53±0.79	1.286±0.58	$\chi2$=0.4407	p=0.506, NS

Note: **= Statistically significant, NS=Non significant

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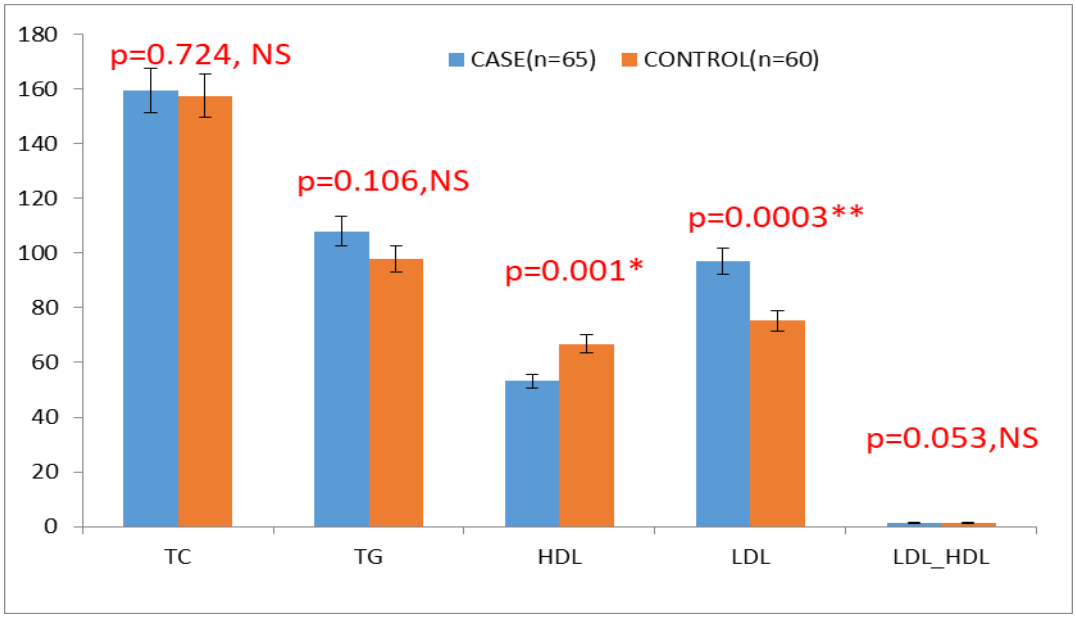

Figure 1: Comparison of lipid profile in control and PCOS subjects.

TC (Total Cholesterol), TG (Triglyceride), HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein).Values are expressed as Mean ± SD, *=Statistically significant, **=Highly significant.

DISCUSSION

Polycystic ovary syndrome (PCOS), the most prevalent hormonal disorders among women of reproductive age is a heterogeneous endocrine and metabolic disorder, causing irregular menstrual cycles, dyslipidaemia, excessive bodyweight, oxidative stress, hyperandrogenism, and infertility[13,14]. PCOS affects 5 to 10% of reproductive-aged women and 40% of affected women experience infertility, making this condition the leading cause of anovulatory infertility [15]. In women with PCOS, the normal ovarian function is disturbed mainly by hyperandrogenism and elevated level of luteinizing hormone (LH) [16], thus resulting in multiple cysts [17].

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in reproductive age women and is associated with both reproductive and metabolic abnormalities. Recent studies have demonstrated an early onset of abnormal cardiovascular risk profile in women with PCOS. Abnormal lipid profile patterns are common in women with PCOS, and these abnormalities are not uniform in all populations. Anthropometry is a simple and commonly used research tool for assessing metabolic risk in women with PCOS. Therefore, this study examined the association of vitamin D with anthropometric parameters and lipid profile in women with PCOS.

In the present study, fasting blood sugar, insulin and HOMA-IR showed significantly high in PCOS patients when compared with the control subjects. Whereas vitamin-D level did not show any significant difference. High Density Lipoprotein was significantly less in PCOS patient, Low-Density Lipoprotein was significantly high in PCOS patients, but total cholesterol, triglyceride and HDL/ LDL ratio did not show any significant variation between case and controls.

In a meta-analysis published earlier showed that 25OHD concentrations of PCOS patients were lower than those of subjects without PCOS and that HOMA-IR was significantly higher in PCOS patients than in women without PCOS, suggesting that serum vitamin D concentration was negatively associated with IR in PCOS [18] . This finding was consistent with our studies revealing a negative association of 25OHD and HOMA-IR in PCOS women. The 25OHD concentration is an indicator of vitamin D status in the human body, and vitamin D deficiency is a major problem in PCOS because it relates to metabolic syndrome, which includes obesity, IR, and glucose intolerance. Our results indicated that women with PCOS had markedly lower 25OHD concentrations, consistent with the findings of previous studies that reported lower vitamin D levels in PCOS patients than in non-PCOS patients [19].

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