

Correlation of vitamin D and Parathyroid hormone with insulin resistance in PCOS women

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Abstract

Aim: To investigate the relation of vitamin D concentration and parathyroid hormone with insulin resistance in PCOS women.

Methods: In the department of Obstetrics and Gynecology at Dr. Baba Saheb Ambedkar Medical College & Hospital, Rohini, Delhi, a one-year observational study was conducted. The levels of 25, hydroxyvitamin D and PTH, as well as the levels of fasting sugar and insulin in the blood, were tested.

Results: There was a 91.0 percent prevalence of vitamin D insufficiency (<20 ng/ml) in the study, whereas 67.9 percent of participants had an elevated parathyroid hormone level.

According to the study, vitamin D insufficiency ($r=-0.64$, $p=0.01$) had a significant negative connection with the HOMA-IR. Increased PTH levels were shown to have a positive correlation with HOMA-IR.

Conclusion: Women with PCOS who have high parathyroid hormone levels or vitamin D insufficiency have a higher incidence of glucose intolerance.

If vitamin D insufficiency and insulin resistance are strongly linked, it may be possible to treat insulin resistance by raising vitamin D levels.

Keywords: PCOS, Vitamin D, Parathyroid hormone, insulin resistance, HOMA-IR

Introduction

A prevalent endocrinopathy affecting women between the ages of 18 and 44 is polycystic ovarian syndrome (PCOS)^[1]. Multiple immature follicles may be visible on ultrasonography as well as excessive androgen levels and menstrual irregularities^[2]. IR and abdominal obesity are common in this condition, putting PCOS women at an increased risk of developing metabolic diseases^[3]. The hormones that regulate calcium homeostasis are altered by obesity, IR, and hyperinsulinemia. Obese adults and women with polycystic ovary syndrome (PCOS)

have lower levels of vitamin D and higher levels of parathyroid hormone (PTH)^[4-6]. The metabolic syndrome and obesity are both associated with changes in vitamin D metabolism and levels of the hormone parathyroid (PTH). Obesity is associated with lower amounts of 25OHD in certain studies, despite a higher surface area to be exposed to sunlight^[7-8]. Insulin resistance is caused in obese PCOS women by an increase in adipose tissue. Reduced adiponectin levels, along with higher levels of free fatty acids in the blood, are associated with obesity, which promotes insulin resistance. In lean women with polycystic ovary syndrome (PCOS), alterations in post-receptor insulin signalling are linked to insulin resistance. Compensatory hyperinsulinemia promotes androgenism via the ovarian synthesis of testosterone.

Vitamin D metabolism is linked to insulin and glucose metabolism, according to a growing body of research. Insulin resistance has been linked to insulin metabolite levels that are too low and PTH levels that are too high^[9]. As the vitamin D response element is found in the promoter region of insulin receptor gene promoter, 1,25OHD directly improves insulin action for glucose transport by promoting the development of insulin receptors^[10]. Increased insulin receptor expression or inhibition of pro-inflammatory cytokines is thought to have a role in insulin resistance, according to some researchers^[11].

As far as we know, this is the first research in the regional population that has examined the effects of calciotropic hormones on insulin resistance and the clinical characteristics of PCOS.

Materials and Methods

This prospective observational study was carried out in the department of Obstetrics and Gynaecology, Dr. Baba Saheb Ambedkar medical college and hospital Rohini Delhi for the period of 1 year, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent, detailed history was taken from the patient.

Methodology

Baseline characteristic of women including age, body mass index (BMI), socioeconomic status and religion was recorded. Total 78 women between 20-50 years, attending the Gynaecology OPD and willing to comply with the study protocol, participated in the study. PCOS women diagnosed by the Rotterdam criteria were included. Rotterdam's criteria is defined as presence of at least two of the three features; anovulation, clinical or biochemical signs of hirsutism or features of polycystic ovaries on pelvic ultrasonography. On ultrasonography, presence of polycystic ovaries were defined by either a volume of at least 10ml or more than 12 follicles (2-9 mm diameter) in at least one ovary. Women with ongoing pregnancy, elevated calcium or prolactin levels, kidney or liver disease, thyroid disorder, or currently using vitamin D supplements were excluded from the study. Ultrasonography was done during the early follicular phase. Ovarian volume was estimated according to the formula $\frac{1}{2} (A \times B \times C)$, where A is the longitudinal diameter, B the antero-posterior diameter and C, the transverse diameter of the ovary. Blood sample was withdrawn after 8 to 10 hours of overnight fasting between days 2 to 5 of menstrual cycle during a spontaneous bleeding episode or progestin-induced menstrual cycle. Serum 25 (OH) D levels and PTH concentration was measured by electro immunoassay. Serum Insulin (fasting) was measured using electro immunoassay. Insulin resistance was estimated using the homeostatic model assessment-insulin resistance (HOMA-IR) and find out association of various parameters with Vitamin D3 and PTH. A p value of <0.05 was considered statistically significant.

Results

Total 78 PCOS women participated in the study. The mean age of the women was 27.18 years and the median of BMI was 24.68 kg/m². Majority of the women had irregular cycle, hirsutism (mFG score ≥ 8) and acne. Median of serum LH was 12.7 IU/ml. 76% had irregular menstrual cycle while acne and hirsutism were present in 49% and 79% of women respectively. Impaired fasting glucose (90-120mg/dl) was present in 74% of women.

The mean fasting serum insulin and fasting serum glucose was 28.91 mIU/ml and 97.1 mg/dl. The range for HOMA-IR was 3.49-14.78 with a median of 7.09. Only 13 women with PCOS had vitamin D in the normal expected range (30ng/ml). Hypovitaminosis D [25(OH)D < 20ng/ml] was present in 91.0% of women with a median level of 25(OH)D was 6.5ng/ml.

Hyperparathyroidism was present in 67.9% of women; with a median of 43.39 pg/ml. Significant association was observed between vitamin D deficiency and menstrual irregularities ($p=0.001$). While no significant association was found between hyperparathyroidism and menstrual irregularities ($p=0.69$). Vitamin D deficiency was significantly associated with obesity and overweight; $p<0.005$. There was negative correlation of vitamin D levels with BMI; $r=-0.51$, $p<0.005$ while no such association was seen with hyperparathyroidism ($r=0.139$, $p=0.306$).

There was significant association between vitamin D deficiency and serum fasting insulin and insulin resistance among PCOS women; $p<0.05$ and $p<0.05$ respectively. There was significant negative correlation with vitamin D levels and fasting sugar, fasting insulin and HOMA IR; $r=-0.29$, $p=0.02$, $r=-0.69$, $p<0.001$, $r=-0.64$, $p<0.01$ respectively. Association with hyperparathyroidism and insulin resistance was not found to be significant ($r=0.53$ $p=0.53$).

Table 1: Demographic profile of patients

Parameters	Women with PCOS (n=78)
	Mean
Age	27.18
BMI (kg/m ²)	24.68

Table 2: Hormonal level with PCOS

Parameters	Women with PCOS (n=78)
S. insulin (μ U/ml)	28.91
S. glucose (mg/dl)	97.1
HOMA-IR	7.09 (3.49-14.78 Range)

Table 3: PTH and vitamin D level in PCOS patients

Parameters	Women with PCOS	(n=78)
PTH (pg/ml)	Normal	25
	Abnormal	53
Hypovitaminosis D [25(OH)D < 20ng/ml]	71	
	25(OH)D was 6.5ng/ml	7

Table 4: Correlation of Vitamin D levels and PTH levels with obesity and IR

Parameter	Vitamin D deficiency	Hyperparathyroidism
BMI	$r=-0.51$, $p<0.005$	$r=0.139$, $p=0.306$
HOMA-IR	$r=-0.64$, $p<0.01$	$r=0.53$ $p=0.53$

Discussion

Gene transcription is hypothesised to have a role in the development of PCOS^[12]. Studies demonstrate that low 25(OH)D levels are linked to insulin resistance, irregular menstruation, hirsutism, hyperandrogenism and obesity, as well as elevated cardiovascular risk factors in women with polycystic ovary syndrome (PCOS)^[13].

This research demonstrated a statistically significant link between menstrual irregularities and hypovitaminosis D ($p=0.001$) in the study group. PTH generation increases when vitamin D insufficiency is present. Vitamin D insufficiency increases PTH production, which is controlled by levels of serum calcium and vitamin D, and elevated PTH is also independently linked to PCOS, anovulatory infertility, and higher testosterone levels^[14].

In our research, 76% of women with PCOS had irregular menstrual cycles. Menstrual irregularity is the most prevalent cause for a gynaecological referral in women with PCOS, according to Ozkan *et al.* (2010)^[15].

The ovary, placenta and endometrium all contain vitamin D receptors. As a result, follicular stoppage and menstrual disruption are common in women with PCOS who are deficient in this vitamin. 13.49 percent of women in the study group had acne and 79 percent of women in the study group had hirsutism (mFG score >8). Women with polycystic ovary syndrome (PCOS) who experience monthly abnormalities may benefit from vitamin D treatment, according to the majority of research.

PCOS is caused in part by an abnormality in calcium homeostasis, which halts follicular growth. During the menstrual cycle, Pitkin *et al.* found that extended menstrual periods may be attributed to PTH^[16].

Menstrual abnormalities were shown to be unrelated to hyperparathyroidism ($p=0.69$) in our research. Women with persistent anovulation had greater PTH levels, according to Thys-Jacob S *et al.*^[17] There haven't been a lot of research done to see whether menstrual abnormalities are linked to an elevated parathyroid hormone level. As a result, more investigation is required to discover this association. One third of women with PCOS suffer from acne, according to Balen *et al.* (2005), and the majority of women with severe acne are also diagnosed with PCOS^[18]. Acne is caused by androgen-induced sebaceous gland hypertrophy in these women^[19].

Vitamin D levels and serum PTH levels were shown to be adversely associated among women with PCOS; however the correlation was not statistically significant.

In contrast, Panidis *et al.*^[14] discovered a negative correlation between vitamin D and Serum PTH among obese women with PCOS; $r = -0.142$, $p = 0.03$. Anovulatory PCOS women also showed a strong negative correlation between them; $r=0.664$, $p=0.00120$. For the lack of study on the association between vitamin D and PTH levels in PCOS patients, further investigations are needed.

It was determined that these women had a variety of indicators of insulin resistance, including fasting blood sugar, fasting insulin, and the HOMA-IR index (insulin resistance).

Vitamin D deficient PCOS patients had substantially higher fasting insulin and HOMA IR than non-PCOS women ($p=0.05$). There was no association between fasting glucose and vitamin D insufficiency or hyperparathyroidism. Women with increased PTH concentrations in PCOS had substantially higher fasting insulin and HOMA IR, with $p<0.05$ and $p=0.002$ respectively. Wehret *et al.* (2009) observed a strong association between vitamin D insufficiency and elevated HOMA IR readings. Also, vitamin D levels and fasting glucose and fasting insulin were shown to have a negative association with each other ($p<0.0001$ for both)^[21].

Mahmoud *et al.* found a strong link between PTH, fasting insulin, and insulin resistance, which is consistent with our findings^[22]. However, Panidis *et al.* found no association between PTH levels and insulin resistance in 291 PCOS patients and 109 healthy controls^[14].

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