

Study the Extent of The Relationship Among Hormonal Disturbance, Vitamin D Deficiency and Age in Women with Polycystic Ovary Thiqar City, Southern Iraq

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Abstract. The goal of this study was to see if there was a link between LH, FSH, testosterone, oestradiol, progesterone, and metabolic markers, including AMH and vitamin D, in a woman. PCOS patients had significant increases in serum levels of LH (P <0.01), FSH (P 0.05), LH/FSH ratio (P <0.05), testosterone (P <0.01), progesterone (P <0.05), antimalaria (P <0.001), glucose (P <0.01), total cholesterol (P 0.01), triglycerides (P <0.001), LDL (P <0.01), VLDL (P <0.05), and Vitamin D (P <0.01). AMH appeared to be favourably connected with higher levels of LH, FSH, LH/FSH ratio, testosterone, progesterone, hyperglycemia, total cholesterol, triglycerides, LDL, and VLDL, and uncorrelated with oestradiol and HDL. We can conclude that AMH can potentially be applicable as a diagnostic marker for PCOS, the results also showed vitamin D deficiency is related to pathophysiology of PCOS. Vitamin D serum levels showed an inverse correlation with hyperglycaemia, hyperlipidaemia, and hormonal disturbances in PCOS.

Keywords: Hormonal disorders, metabolic disorders, PCOS, Vitamin D, AMH

1 Introduction

PCOS is a complicated endocrine condition that affects women of reproductive age and is thought to be the leading cause of infertility due to anovulation. [1-2]. It has been described as a syndrome characterised by oligomenorrhea and polycystic ovaries, as well as hirsutism, acne, and obesity [3]. Excess secretion of androgen associated with changes in ovarian morphology represented the main pathological factor in PCOS. Hyperlipidaemia, insulin resistance, and psychosocial dysfunction are part of the symptoms and signs of PCOS [4]. PCOS is diagnosed by the presence of oligo amenorrhoea, polycystic ovaries morphology, and hyperandrogenaemia [5].

Anti-Mullerian hormone (AMH), a glycoprotein secreted by the granulosa cells of ovarian early developing follicles, has also been used in the diagnosis of PCOS [6]. PCOS is defined by an overabundance of tiny antral follicles in the ovaries and high levels of AMH in the blood [7]. Vitamin D insufficiency is frequent among women with PCOS, according to numerous research [8]. Low vitamin D levels were linked to menstrual abnormalities, ovulation issues, and

infertility [9-10]. Vitamin D insufficiency has also been linked to increased insulin resistance and other factors [10-11]. Vitamin D receptors were found in a variety of human tissues, including the ovary and endometrial, indicating that vitamin D plays an active function in female reproductive organs [12-13]. The researchers wanted to see if there was a link of serum vitamin D levels, hormonal irregularities, and age in individuals with PCOS.

2 Materials and Methods

Fasting of 60 blood samples were composed from married infertile women (20-40 years) with PCO attending Al-Shatra hospital, Bint AL-Hoda, and Al-Husseini teaching hospital in Thi-Qar governorate- Iraq, who diagnosed by gynaecologists, through the period from 1 September 2020 until the end of November 2020. Patients with androgen-secreting tumours, hyperprolactinemia, The study excluded women with Cushing syndrome, congenital adrenal hyperplasia, contraceptives, hypoglycemic drugs, lipid-lowering therapy, or hormonal prescriptions. To serve as a control, fasting blood samples were taken from 30 healthy non-pregnant women of similar ages. The study was permitted by Thi-Qar governorate's health directorate and the South technical university's ethical board. All participants gave their informed consent. Glucose and lipid profile were determined by using Cobas C311 photometric assays and ion-selective electrode measurements (Kits and instrument Roche- Germany), while, LH, FSH, oestradiol, progesterone, testosterone, AMH, and vitamin D were determined by using Cobas 411 immunoassay analysis (Kits and instrument Roche- Germany) [14-15]. All data is presented as a mean \pm SE. Student t-tests were used to analyse differences in mean values for specific hormone measures.

3 Results

In the group aged 20-25 years, PCO patients showed significantly elevated serum levels. While the serum level of oestradiol, HDL cholesterol, and vitamin D were significantly declined. Table 1 shows vitamin D levels were positively connected with oestradiol and HDL cholesterol while being negatively correlated with LH, FSH, LH/FSH ratio, total testosterone, progesterone, AMH, hyperglycemia, total cholesterol, triglycerides, and VLDL cholesterol.

Table 1: Data in PCOS patients aged 20-25 years in comparison with aged-matched control.

Parameter studied		Control (15)	PCOS patients (37)	Significance
LH (IU/L)		4.99±0.62	15.86±0.96	P< 0.001
FSH (IU/L)		3.42±0.32	4.68±0.45	P< 0.05
LH/FSH		1.45±0.08	3.38±0.12	P< 0.05
Total testosterone (ng/ml)		0.46±0.08	0.58±0.06	P< 0.05
Oestradiol (pmol/l)		116.64±8.62	106.33±9.32	P< 0.05
Progesterone (nmol/ml)		0.67±0.06	1.44±0.09	P< 0.05
AMH(ng/ml)		2.40±0.12	10.00±0.23	P< 0.001
Glucose (mg/dl)		94.60±3.23	109.02±4.32	P< 0.05
Lipid profile	Total cholesterol (mg/dl)	170.00±6.16	176.00±7.22	P< 0.05
	Triglycerides (mg/dl)	150.66±5.56	175.81±6.32	P< 0.01
	LDL (mg/dl)	98.81±3.51	97.17±4.12	NS
	VLDL (mg/dl)	30.76±1.45	35.18±1.94	P< 0.05
	HDL (mg/dl)	48.93±1.66	45.91±1.57	P< 0.05
Vitamin D (ng/ml)		16.95±0.96	14.26±0.84	P< 0.05

In the group aged 26-30 years, serum biochemical analysis of PCO patients revealed significant elevation of serum levels were illustrated. While the serum level were significantly declined in comparison with control. As indicated in Table 2, vitamin D levels were positively connected with oestradiol testosterone and HDL cholesterol, but negatively correlated with LH, FSH, LH/FSH, total testosterone, AMH, hyperglycemia and etc.

Table 2: Similar to Table 1 but for patients aged 26-30 years.

Parameter studied		Control (6)	PCOS patients (11)	Significance
LH (IU/L)		5.67±	9.58±	P< 0.01
FSH (IU/L)		3.79±	5.37	P< 0.05
LH/FSH		1.49±	1.78±	P< 0.05
Total testosterone (ng/ml)		0.42±	0.48±	P< 0.05
Oestradiol (pmol/l)		107.90±	74.33±	P< 0.05
Progesterone (nmol/ml)		0.84±	0.76±	NS
AMH(ng/ml)		5.35±	8.96±	P< 0.01
Glucose (mg/dl)		97.80±	101.00±	P< 0.05
Lipid profile	Total cholesterol (mg/dl)	190.00±	196.00±	P< 0.05
	Triglycerides (mg/dl)	184.00±	211.50±	P< 0.01
	LDL (mg/dl)	91.00±	99.70±	P< 0.05
	VLDL (mg/dl)	41.20±	45.60±	P< 0.05
	HDL (mg/dl)	53.80±	40.72±	P< 0.01
Vitamin D (ng/ml)		21.96±	17.28±	P< 0.05

In PCO non-control aged 31-35 years, serum levels of LH were considerably higher. Serum levels of oestradiol were significantly lower in the experimental group than in the control group. Vitamin D levels were positively related to oestradiol and HDL cholesterol, but negatively related to LH, FSH, LH/FSH, as indicated in Table 3.

Table 3: Similar to Table 1 but for patients aged 31-35 years.

Parameter studied		Control (5)	PCOS patients (7)	Significance
LH (IU/L)		4.13±0.31	11.17±0.73	P< 0.001
FSH (IU /L)		3.44±0.05	4.71±0.08	P< 0.05
LH/FSH		1.20±0.05	2.37±0.06	P< 0.01
Total testosterone (ng/ml)		0.47±0.02	0.55±0.03	P< 0.05
Oestradiol (pmol/l)		119.32±4.62	90.39±3.78	P< 0.05
Progesterone (nmol/ml)		0.37±0.03	0.54±0.04	P< 0.05
AMH(ng/ml)		2.41±0.07	11.27±0.26	P< 0.001
Glucose (mg/dl)		82.00±3.54	113.857±6.23	P< 0.05
Lipid profile	Total cholesterol (mg/dl)	198.00±7.82	205.00±9.63	P< 0.05
	Triglycerides (mg/dl)	200.00±8.82	257.85±10.64	P< 0.001
	LDL (mg/dl)	101.25±3.62	105.83±3.82	P< 0.05
	VLDL (mg/dl)	44.50±1.28	56.83±1.64	P< 0.05
	HDL (mg/dl)	58.00±2.68	42.00±1.98	P< 0.01
Vitamin D (ng/ml)		20.51±2.82	14.96±1.64	P< 0.01

PCO patients aged 31-35 years had significantly higher serum levels when compared to the control group. The serum levels of oestradiol, on the other hand, all decreased significantly. Vitamin D levels were linked with oestradiol and HDL cholesterol, but adversely associated with LH, FSH, LH/FSH, total testosterone, AMH, hyperglycemia, total cholesterol, triglycerides, and LDL cholesterol, as indicated in Table 4.

Table 4: Similar to Table 1 but for patients aged 36-40 years.

Parameter studied		Control (4)	PCOS patients (5)	Significancy
LH (IU/L)		6.54±0.42	10.32±0.85	P< 0.01
FSH (IU/L)		4.40±0.12	5.28±0.24	P< 0.05
LH/FSH		1.48±0.12	2.03±0.15	P< 0.05
Total testosterone (ng/ml)		0.52±0.06	0.68±0.08	P< 0.05
Oestradiol (pmol/l)		92.00±4.62	60.00±3.32	P< 0.01
Progesterone (nmol/ml)		0.82±0.06	0.84±0.04	NS
AMH(ng/ml)		1.47±0.09	3.90±0.13	P< 0.01
Glucose (mg/dl)		104.66± 4.58	165.40±6.51	P< 0.001
Lipid profile	Total cholesterol (mg/dl)	180.00±8.72	227.00± 12.64	P< 0.001
	Triglycerides (mg/dl)	156.66±8.62	210.00±10.28	P< 0.001
	LDL (mg/dl)	127.25±6.23	142.20±7.52	P< 0.01
	VLDL (mg/dl)	45.33±6.43	47.25±6.67	NS
	HDL (mg/dl)	46.00±2.12	42.80±1.23	P< 0.05
Vitamin D (ng/ml)		29.11±1.34	14.84±0.98	P< 0.01

4 Discussion

All tables showed that the results of all age subgroups of the control group were similar, furthermore the results of all age subgroups in PCO patients were also identical. The results agreed with many previous studies [16], [17], [18], which mentioned that there were no variations in the level of pathological markers among age groups in PCO women. The hormonal disturbances recorded in PCOS in this study could be attributed to hypothalamic dysfunction. Hypothalamic dysfunction may be a primary or secondary cause of abnormal steroid feedback. In either case serum LH level, rises and increased levels are observed clinically in approximately 50% of PCOS women [19]. In roughly 60% of individuals with PCOS [20], the ratio between FSH and LH levels, which is ordinarily around 2 to 1, becomes reversed and occasionally even higher (2 or 3 to 1) as a result of this derangement [20], as shown in the current study. Increased androgen production is caused by an increase in LH hormone, which is further boosted by insulin resistance associated with this disease [21].

The current study showed that AMH was positively correlated with the elevated LH, FSH, LH/FSH ratio, testosterone, progesterone, glucose, and lipid profile and negatively correlated with oestradiol, and HDL. While vitamin D was negatively correlated with AMH. These results agreed with many studies [22], [23], [24]. In addition, giving vitamin D tablets to PCOS patients restored their serum AMH levels [23], [24].

Vitamin D deficiency was discussed in which greater levels of total testosterone and dehydroepiandrosterone sulphate in PCOS patients [25], [26]. Deficiency was connected to higher levels of LH, FSH, LH/FSH ratio and etc.

Vitamin D receptors (VDRs) have been found in a variety of human tissues, including the ovary and endometrium, proposing vitamin D roles in female reproductive tissues [26], [27], [28]. PCOS has been associated to metabolism of calcium and phosphate, as well as low vitamin D levels [26] [29].

25(OH) D has been identified in women with PCOS in numerous investigations, ranging from 11 to 31 ng/ml, of (67–85 percent) having values below 20 ng/ml. Many research [30], [31] have proven the link between vitamin D levels and excessive LH and testosterone, as well as PCOS symptoms (infertility, hirsutism, and insulin resistance).

Vitamin D helps to boost the activity of steroidogenic enzymes such 3 β -HSD. The corpus luteum is formed by luteinized human granulosa cells throughout the menstrual cycle, which produces a lot of progesterone (and a few oestrogens) and causes endometrial changes such decidualization in order to sustain a pregnancy. Increased progesterone synthesis by 1,25-dihydroxy vitamin D₃ potentiates granulosa cell luteinization, resulting in a healthier endometrial environment [24].

In contrast, vitamin D is associated to many factors of which are common in PCOS and have been linked to ovulatory dysfunction [31], [32]. After supplementing PCOS patients with vitamin D, they showed an improvement in insulin sensitivity [33], [34].

5 Conclusion

Vitamin D insufficiency and PCOS pathogenesis are clearly linked, according to the research. In PCOS patients, vitamin D may play a role in the development of hormonal and metabolic problems. Furthermore, vitamin D's ovarian action may encourage its usage as an adjuvant medication in the treatment of PCOS.

Ethical considerations

The ethics committee of the Thi-Qar governorate's health directorate, as well as the ethical board of the South technical university in Iraq, gave its approval to the study.

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