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THE RELATIONSHIP OF VITAMIN D WITH THE REGULARITY OF THE MENSTRUAL CYCLE IN INFERTILE WOMEN

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Abstract

Vitamin D affects infertility among women. Via vitamin D, were tested in 60 women with infertility and 40 control group. The results showed a low significant elevation in the concentration of Vit. D in infertile women, compared to the healthy women at a significant level of (P = 0.001). The results also showed a significant decrease in the level of the vitamin in infertile women compared with healthy women (control group) at a probability level (P = 0.01) for all age groups, the age is a major factor affecting vitamin D levels, and the elderly are usually more vulnerable to vitamin D deficiency due to the decrease in the skin's production of vitamin D with age and fertility decreases, especially at the age more than of 35 due to the decrease in the egg quantity and quality, as an egg is sent from the ovaries to the female's uterus every month from the time of puberty to menopause. The level of vitamin in infertile women with a regular menstrual cycle is higher compared to infertile women with an irregular menstrual cycle, as this indicates the possibility of vitamin D deficiency, one of the factors that affect the regularity of the cycle of menstruation. This vitamin had a strong positive relationship with Irregular menstruation for different age groups. Finally, the result revealed vitamin D as a new indicator of increasing infertility and miscarriage risk for women.

Keywords: Infertility, Vitamin D, Miscarriage, menstruation, age.

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علاقة فيتامين D مع انتظام الدورة الشهرية لدى النساء المصابات بالعقم*

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نبذة مختصرة:

ركزت الدراسة على فيتامين D و علاقته مع انتظام الدورة الشهرية و زيادة الاصابة بالعقم لدى النساء، حيث تم جمع 60 عينة لنساء مصابات بالعقم و 40 عينة كمجوعة سيطرة. أظهرت النتائج انخفاض معنوي في تركيز فيتامين D عند النساء المصابات بالعقم ، مقارنة بالنساء السليمات عند مستوى احتمالية (P = 0.001) كما أظهرت النتائج انخفاضًا معنويًا في مستوى فيتامين D لجميع الفئات العمرية للنساء المصابات بالعقم مقارنة بالنساء السليمات عند مستوى احتمالية (P = 0.01)، والعمر عامل رئيسي يؤثر على مستويات فيتامين D، وعادة ما يكونن النساء كبار السن أكثر عرضة لنقص فيتامين D بسبب انخفاض إنتاج الجلد للفيتامين مع تقدم العمر وانخفاض الخصوبة، خاصة بعد سن 35 بسبب انخفاض عدد ونوعية البويضات، حيث يتم إرسال البويضة من المبيض إلى رحم الأنثى كل شهر من وقت البلوغ إلى سن اليأس. كما اظهرت الدراسة ان مستوى فيتامين D عند النساء المصابات بالعقم مع الدورة الشهرية المنتظمة أعلى مقارنة بالنساء المصابات بالعقم و اللواتي يعانين من عدم انتظام الدورة الشهرية ، حيث يشير ذلك إلى احتمال نقص فيتامين D هو أحد العوامل التي تؤثر على انتظام الدورة الشهرية. كما ظهر ان لفيتامين D علاقة إيجابية قوية مع عدم انتظام الدورة الشهرية لمختلف الفئات العمرية. أخيرًا ، و اثبتت الدراسة ان فيتامين D علامة دالة جديدة لزيادة مخاطر العقم والإجهاض لدى النساء خاصة مع اضطرابات الدورة الشهرية لكافة الفئات العمرية.

الكلمات الدالة: العقم ، فيتامين D، الإجهاض ، الدورة الشهرية، العمر.

*مستل من رسالة ماجستير الباحث الاول.

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Introduction:

Infertility is a widespread health issue worldwide and is considered to be the failure to conceive either after treatment or in the case of using fertilization methods outside the body after one year or more of marriage (Al-Taie & Al-jawadi 2019; Jungwirth *et al.*, 2012) and the scientist Hippocrates is the first to He wrote about infertility cases and attributed to him a diagnosis of infertility as a disease (Cong *et al.*, 2016).

The emergence of a huge data in the past ten years on the global prevalence of vitamin D deficiency, especially in the Middle East, justifies taking this issue seriously and preparing to resolve the health problems associated with vitamin D deficiency (Miyashita *et al*., 2016). Also, deficiencies will influence health status for both mother and fetus has recently drawn attention because of the reason that vitamin D may have a role in production and fertilization and its deficiency, which has become an epidemic of the era (Sayegh *et al.*, 2014), and it was there a growing interest in researching the Vit. D correlation of deficiency and infertility in recent years. Therefore, there is an urgent need for further studies using reference methods to directly determine the level of vitamin D to confirm its role in the treatment of female infertility, to confirm the causal relationship, and to research the possible therapeutic effects of supplementation with vitamin D (Cie´sli nska *et al.*, 2018).

Materials and Methods:

Group of Infertile Patients: Sixty infertile women have been registered in this research, it was diagnosed by specialists in Hospitals, and a laboratory test was done in the laboratories of the hospitals, in addition to external laboratories for the period from13/9/2019 to 17/5/2020. Their ages are between 18-45 years, and clinical data were obtained for each case in a questionnaire prepared for this purpose. Excluded conditions include diabetes, high blood pressure, and thyroid disease. Control Group: This study was attended by forty young fertile women (control group), ages ranging from 17-45 years.

The two groups were tested from blood after a 12-hour fasting, early follicular cycles (cycle days 2 or 3) for vitamin D in the test tube and centrifuged for serum separation within an hour of blood collection, and the serum was stored in a deep freezer at a temperature of -20^{o}C for subsequent analysis. Samples were analyzed in batches of 100 to be omitted between analytical variations. Samples were permitted to reach room temperature before the study. The commercial kits (Roche kits) were then measured by Cobas e411. Paragraph comes content here. Paragraph comes content here. Paragraph comes content here.

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Ethical approval:

The research has been carried out and agreed upon by the author's Institutional Review Board by all applicable national legislation, institutional policy, and the values of the Helsinki Declaration.

Statistical analysis:

SPSS software has been used to analyze the data. The T-test and Duncan tests were already used to compare parameters between the total control number and patients based on occupancy at $p \leq 0.05$, $p \leq 0.01$, and $p \leq 0.001$, respectively, and the test of Pearson correlation coefficient (Kirkpatrick & Feeney, 2012).

Results:

The results shown in Table-1 showed a significant decrease in the level of vitamin D at a probability level of (0. 001 = P), in infertile women compared to healthy women, which is usually responsible for stimulating sexual desire in addition to the fact that Vit. D deficiency is common in women. Those with a premature ovarian deficiency (Wasiewicz *et al.*, 2018).

In addition, Vit. D deficiency is associated with premature ovarian failure and is characterized by menopausal disorder, lack of metabolism, and high levels of serum gonads in females it under the age of forty, and it has also been noted that low vitamin D is associated with an increased likelihood of miscarriage as it increases the likelihood of preeclampsia (Voulgaris *et al.*, 2017).

Table -1: Vitamin D level for infertile women (primary and secondary) compared with healthy women (control group).

Cases	**Vit. D (ng/dL) Mean±SD**
Healthy women (control group)	39.94 ± 6.46
Primary infertile women	11.94 ± 5.82
Secondary infertile women	11.83± 5.78
p-value	0.001***

The results showed clear results in Table-2 a significant decrease in the level of Vit. D in infertile women compared with the group of healthy women (control group) at a probability level (P = 0. 01) for all age groups, where the proportion of the vitamin in women with infertility depends mainly on Social habits, degree of exposure to sunlight, obesity, and health factors for women. Age is a major factor that affects vitamin D levels. The elderly are usually more vulnerable to the Defect of vitamin D due to the reduction of vitamin synthesis in the skin with age, in addition to a decrease in skin thickness and weakness. Intestinal absorption and lower liver and kidney hydroxylase (Atteritano *et al.*, 2018). Vitamin D concentration is negatively renal connected follicle-stimulating hormone levels in premenopausal women and this indicates that Vitamin D may influence ovarian reserve, and thus may It has effects on fertility in women with age (Lips *et al.*, 2014) and has demonstrated that endometriosis is capable of synthesizing vitamin D which is transformed through endometrial receptors and modifying gene expression or regulating response. For immunity, as the endometrium produces calcitriol which is a functional form of the vitamin in addition to the fetus upon entering the uterine cavity shortly before implantation, calcitriol controls many genes involved in the implantation of embryos. Once a woman becomes pregnant, the uterus and placenta continue to produce calcitriol, which helps regulate the immune cells in the uterus so that the infection can be fought without compromising the pregnancy and that fertility in women is closely related to an adequate concentration of vitamin D (Mahmoudi *et al.*, 2015; Reid *et al.*, 2014) Adequate vitamin D levels are essential for a successful pregnancy in addition to the sex steroid hormones that regulate reproduction (Farzadi *et al.*, 2015).

Table-2: Comparison of Vitamin D level in infertile women with different age groups.

Age groups	**NO.**	**Vit. D (ng/dL) Mean±SD**
(18-24) year	19	14.68 ± 9.82b
(25-31) year	22	13.446 ± 6.07b
(32-38) year	12	11.81 ± 5.36b
(39-45) year	7	9.950 ± 3.17b
p-value		0.01*

The results shown in figure -1 showed the level of the vitamin in infertile women with a regular menstrual cycle higher compared to sterile women with an irregular menstrual cycle, as this indicates the possibility of vitamin D deficiency, one of the

factors that affect the regularity of the menstrual cycle and this is in agreement with a recent study in 2020 (Grieger & Norman, 2020) though some of the signals that a woman is really not ovulating usually include irregular periods of menstruation, as well as that many instances of infertility arise due to issues with ovulation, and have been no eggs that are fertilized. Epidemiological evidence also confirmed the negative impact of obesity on female reproduction, including irregular ovulation and menstruation, and this is consistent with what Faust and his group found in 2019 (Faust *et al.*, 2019).

The female menstrual cycle is linked to a series of modifications which happen in the uterus and ovaries, which leads to ovulation and the shedding of the endometrium when no-pregnancy occur and is caused by the interaction of many hormones produced by the pituitary anterior gland and the ovaries, including FSH and LH, estrogen hormone and progesterone hormone, the menstrual cycle begins with menstruation and is divided by two bands: the follicular (pre-ovulation) and the luteal (postovulatory) zone (Khayyatzadeh *et al.*, 2017). And that the low level of the vitamin is associated with symptoms of insulin resistance and ovulation disorders that can lead to infertility and PCOS, and from this, conclude that vitamin D deficiency appears as the risk factor for menstrual disturbance and irregularity (Moini *et al.*, 2015).

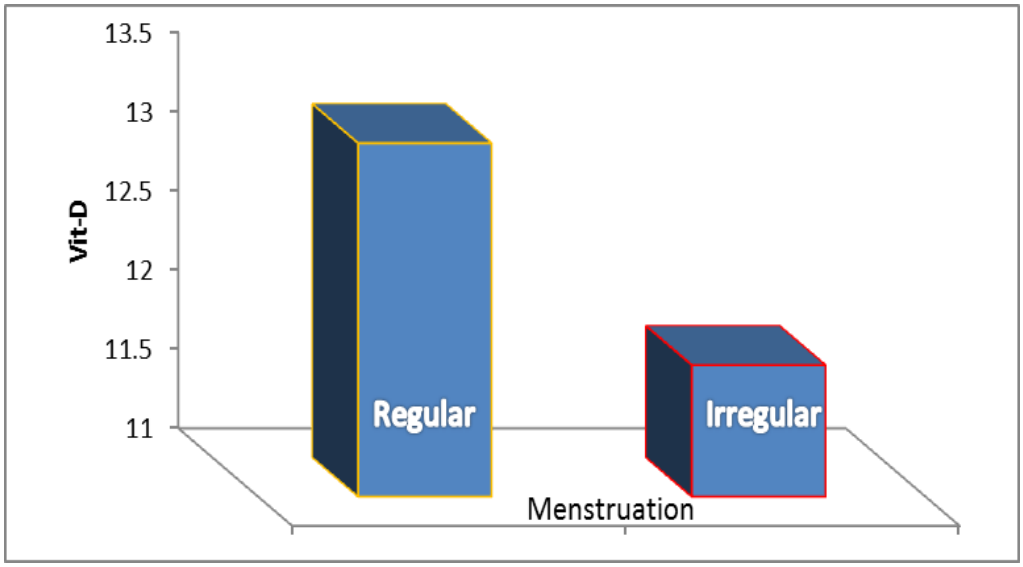

Figure -1: The relationship of vitamin D with the regularity of the menstrual cycle in infertile women.

Conclusion:

This study found that vitamin D is a new marker for increasing infertility in women associated with irregular menstruation and for different age groups, so the

primary goal should be to manage these women before starting any treatment to correct their hormonal imbalance by measuring their level and vitamin D and regulating the menstrual cycle under medical supervision before planning a pregnancy.

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