Section: Biochemistry

Original Research Article

A STUDY OF ASSOCIATION BETWEEN VIT D & B12 DEFICIENCY AND HUMAN FERTILITY IN REPRODUCTIVE-AGED WOMEN

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Abstract

Background: To investigate the relationships between 25(OH)D & Vit-B12 levels and human fertility in healthy reproductive age women. **Materials and Methods:** It was a cross-sectional study; Study conducted in the department of biochemistry MGM Medical College & LSK Hospital, Kishanganj, Bihar. One hundred healthy reproductive age women were enrolled in the study, aged between 18 to 25. Hypogonadism was defined as total T(Testosterone) <15 ng/dl. The 25(OH)D, FSH, LH, and E2 were measured using chemiluminescence. The associations between 25(OH)D and reproductive hormones and hypogonadism were analyzed using linear regression analyses. **Results:** We have found in our study, the negative correlation between AMH &Vit-D and B12, r factor -.389 &-.529 p value was <0.05. And type of sensitivity of AMH with (LH, FSH, PRL, E2, Testosterone,) and P value <0.05 of linear regression between AMH and the following variables (LH, FSH, Testosterone, & PRL,). **Conclusion:** This study to compare total 25(OH)D and Vitamin-B12 in a relatively large cohort of healthy reproductive age women. Total vitamin D showed similar correlations with endocrinological parameters, i.e. inverse correlations with free androgen index, luteinizing hormone, testosterone, LH/FSH ratio, and anti-Müllerian hormone, and also with biochemical parameters.

INTRODUCTION

Women of childbearing age have a disproportionately high rate of vitamin D insufficiency.[1] Vitamin D's physiological function in reproduction is still up for debate. The role of vitamin D in reproduction was first highlighted by studies of rats with 25(OH)D insufficiency, who demonstrated abnormal mating behaviour, decreased fertility, smaller litter sizes, and impaired neonatal growth.[2] Preeclampsia.[3] gestational diabetes mellitus.[4] small for gestational age.[5] and low birth weight.[6] are all conditions that have been linked to poor maternal vitamin D status in humans.[6]

There's only one vitamin D receptor (VDR) that does all the work, and it's been found all over the place in female reproductive organs.[7] Vitamin D insufficiency has been linked to changes in insulin secretion and insulin resistance, according to a number of studies. One of the most frequent endocrine illnesses affecting women of reproductive age is polycystic ovary syndrome, which is characterised by insulin resistance.[8]

Total 25(OH)D levels are currently the gold standard for determining vitamin D status in clinical settings. About 85–90% of serum 25(OH)D is bound to its specific carrier–vitamin D binding protein (DBP), 10–15% is bound to serum albumin, and less than 0.1% exists as totally free unbound form.[9] Only the free form of vitamin D, which can freely traverse the lipophilic cell membrane and connect with the nuclear vitamin D receptor, has any biological effect. DBP concentrations, in turn dependent on liver and kidney health, endocrine condition, and even race, influence total vitamin D concentrations more than mineral-bone metabolism.[10] As a result, the aforementioned confounding factors mean that total vitamin D concentrations may not accurately reflect vitamin D status. A more accurate indicator of vitamin D levels may be free 25(OH)D.[11] Recent research supports this theory.[12]

Objective

To investigate the relationships between 25(OH)D levels and reproductive hormones during adolescent.

MATERIALS AND METHODS

It was a cross-sectional study; Study conducted in the department of biochemistry MGM Medical

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College & LSK Hospital, Kishanganj, Bihar. One hundred reproductive aged women were enrolled in the study, aged between 18 to 25. Hypogonadism was defined as total T(Testosterone) <15 ng/dl. The 25(OH)D, FSH, LH, and E2 were measured using chemiluminescence. The associations between 25(OH)D and reproductive hormones and hypogonadism were analyzed using linear regression analyses.

Methodology

Blood samples taken from (100) reproductive aged women and selected high AMH level patients and also performed ultra sound scan and found polycystic ovaries distributed on the periphery of the ovarian cortex (PCOS pattern ovaries), furthermore 100 women divided into two groups. Group- A- 40 women had AMH level high, and Group- B-60 women had normal AMH level The vitamin D3, vitamin B12, and main infertility hormones (LH, FSH, Testosterone, Prolactin and E2) were estimated in both groups.

RESULTS

This study looks at how Vit-D, B12, affect infertile women with high AMH and polycystic ovaries who are between 14 and 18 years old. The total number of adolescent is the same as the number of girl who have been high AMH level. 40 women with high levels of AMH had their D3, B12, levels estimated. 60 women with normal levels of AMH were used to estimate D3, B12, Those patients' blood samples were drawn on the second to fifth day of the cycle.

Table 1: Person correlation between Higher AMH with Vitamin-D3 & B12 (n=40)

AMH	Vit-D3	VitB12
Pearson Correlation	-389**	-529**
p Value	.002	.000

Table 2: Person correlation between Normal AMH with Vitamin-D3 & B12 (n=60)

AMH	Vit-D3	VitB12
Pearson Correlation	-411	.178
p Value	.06	.109

This study looks at how D3, B12, affect infertile women with high AMH and polycystic ovaries who are between 14 and 18 years old. The total number of adolescent is the same as the number of women who have been high AMH level. 40 women with high levels of AMH had their D3, B12, levels estimated. 60 adolescent girl with normal levels of AMH were used to estimate D3, B12, Those patients' blood samples were drawn on the second to fifth day of the cycle.

Table 3: Linear Regression between other investigation with AMH

Variables	P value	Significant
LH	0.016	S
FSH	0.032	S
PRL	0.001	S
E2	0.423	NS
Testosterone	0.002	S

The table above (3) shows the type of sensitivity of AMH with (LH, FSH, PRL, E2, Testosterone,) and P value <0.05 of linear regression between AMH and the following variables (LH, FSH, Testosterone, & PRL,).

DISCUSSION

In this cross-sectional analysis, researchers compared free 25(OH)D to total 25(OH)D in healthy women of reproductive age. There was a strong relationship between total vitamin D and free vitamin D levels. Similar associations were found between the two and endocrinological and haematological markers associated with reproduction.

Increasing evidences reveal that vitamin D may play a significant function in controlling female fertility.[13] Low vitamin D level is related with unfavourable maternal and foetal outcomes.[3] and is involved in the development of particular gynaecological diseases that influencing fertility, such as endometriosis and polycystic ovarian syndrome (PCOS).[14] Several animal and human investigations have associated vitamin D metabolism with sex steroid production.[15] In the present study we discovered that both total and free 25(OH)D were inversely connected with FAI, LH, total testosterone, AMH, androstenedione, TSH, and positively correlated with SHBG in reproductive-age women.

It is a key finding of the current study that laboratory values depicting total testosterone and androstenedione are among the parameters with the largest negative connection between either free or total vitamin D in reproductive-age Caucasian women. Testosterone has been thoroughly investigated in male, and strong evidence supports the influence of vitamin D on semen quality through the regulation of calcium metabolism and testosterone production.[15] However, few research have focused on the effects of vitamin D on

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testosterone in women. Our results demonstrated that both total and free 25(OH)D were adversely linked with testosterone. Our data are in agreement with another study showing a negative correlation between total 25 (OH)D and free T as well as total T in the follicular fluid of healthy women and with a meta-analysis of studies in women with PCOS.[16] showing likewise an inverse relationship of testosterone to total vitamin D. There is, however, a tiny study in healthy women demonstrating a favourable connection between androgens and total vitamin D.[17] Given the size of this study - eight times smaller than our study and the other studies in PCOS women and the study assessing ovarian fluid, see above, it is more likely that this small study was simply underpowered.

From a biological standpoint, both androgens and vitamin D belong to the steroid family. As noted above, we report a negative connection between laboratory markers defining androgens and vitamin D. A plausible explanation of such a correlation could be drawn from the ability of vitamin D to act as a regulator of a number of enzymes involved in the regulation of the synthesis of adrenal steroid hormones including adrenal androgens as well as ovarian sex hormones.[18] Sex hormones are created in the gonads either by in situ synthesis from cholesterol or by enzyme catalysed conversion of androstenedione or DHEA which are discharged to the circulation from the adrenal gland. Androgens (e.g. testosterone) are created by processes catalysed by 17β-hydroxysteroid dehydrogenase (17β-HSD). The expression of this enzyme was reported to be controlled by 1α,25-dihydroxyvitamin D3 in human prostate cell lines and keratinocytes.[19] Moreover, 1α,25-dihydroxyvitamin D3 was shown to exert tissue-specific effects on androgen metabolism where it led to enhanced androgen production in breast cancer cells, but, dihydrotestosterone generation was lowered in adrenocortical cells treated with 1α,25-dihydroxyvitamin D3.[20]

Our clinical observational findings raise the possibility that vitamin D therapy could help women with hyperandrogenism by enhancing their endocrine condition. However, two meta-analyses have found contradictory data with respect to the effect of vitamin D treatment on androgens in women with PCOS.[21] There are two possible explanations for this. Total vitamin D levels were used to assess vitamin D status in these investigations. Second, it is not known what the ideal doses are for enhancing human androgen status. Proper dose discovery studies would be needed. Yet this was not carried out. It is still unknown what vitamin D concentrations would result in optimal androgen status, fertility rate, and embryo development in humans. In addition to increased androgens, PCOS is also characterised by increased luteinizing hormone (LH) and antimüllerian hormone (AMH).[22] Both also have a negative relationship with both free and total vitamin D. This again underscores the likely necessity of vitamin D to optimise the endocrine state in women with PCOS. Dose-finding trials with appropriate designs are needed for this, as was noted above.

CONCLUSION

This study to compare total 25(OH)D and Vitamin-B12 in a relatively large cohort of healthy reproductive age women. Total vitamin D showed similar correlations with endocrinological parameters, i.e. inverse correlations with free androgen index, luteinizing hormone, testosterone, LH/FSH ratio, and anti-Müllerian hormone, and also with biochemical parameters.

Conflicts of Interests Nil
Authors Contribution Equal contribution
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REFERENCES

1. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J ClinEndocrinolMetab (2011) 96:1911–30. doi: 10.1210/jc.2011-0385.
2. Kwiecinksi GG, Petrie GI, DeLuca HF. 1,25-Dihydroxyvitamin D3 restores fertility of vitamin D-deficient female rats. Am J Physiol (1989) 256:E483–7. doi: 10.1152/ajpendo.1989.256.4.E483.
3. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J ClinEndocrinolMetab (2007) 92:3517–22. doi: 10.1210/jc.2007-0718.
4. Poel YH, Hummel P, Lips P, Stam F, van der Ploeg T, Simsek S. Vitamin D and gestational diabetes: a systematic review and meta-analysis. Eur J Intern Med (2012) 23:465–9. doi: 10.1016/j.ejim.2012.01.007
5. Gernand AD, Simhan HN, Klebanoff MA, Bodnar LM. Maternal serum 25- hydroxyvitamin D and measures of newborn and placental weight in a U.S. multicenter cohort study. J ClinEndocrinolMetab (2013) 98:398–404. doi: 10.1210/jc.2012-3275
6. Gernand AD, Bodnar LM, Klebanoff MA, Parks WT, Simhan HN. Maternal serum 25-hydroxyvitamin D and placental vascular pathology in a multicenter US cohort. Am J ClinNutr (2013) 98:383–8. doi: 10.3945/ajcn.112.055426
7. Ciepiela P, Duleba AJ, Kowaleczko E, Chelstowski K, Kurzawa R. Vitamin D as a follicular marker of human oocyte quality and a serum marker of in vitro fertilization outcome. J Assist Reprod Genet (2018) 35:1265–76. doi: 10.1007/ s10815-018-1179-4
8. Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. ClinEndocrinol (Oxf) (2012) 77:343–50. doi: 10.1111/j.1365-2265.2012.04434.x.
9. Tsuprykov O, Chen X, Hocher CF, Skoblo R, Lianghong Y, Hocher B. Why should we measure free 25(OH) vitamin D? J Steroid BiochemMolBiol (2018) 180:87–104. doi: 10.1016/j.jsbmb.2017.11.014
10. Bikle DD, Gee E, Halloran B, Kowalski MA, Ryzen E, Haddad JG. Assessment of the free fraction of 25-hydroxyvitamin D in serum and its regulation by albumin and the vitamin D-binding protein. J ClinEndocrinolMetab (1986) 63:954–9. doi: 10.1210/jcem-63-4-954.
11. Mendel CM. The free hormone hypothesis: a physiologically based mathematical model. Endocr Rev (1989) 10:232–74. doi: 10.1210/edrv-10-3-232

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12. Johnsen MS, Grimnes G, Figenschau Y, Torjesen PA, Almas B, Jorde R. Serum free and bio-available 25-hydroxyvitamin D correlate better with bone density than serum total 25-hydroxyvitamin D. Scand J Clin Lab Invest (2014) 74:177–83. doi: 10.3109/00365513.2013.869701.
13. Anagnostis P, Karras S, Goulis DG. Vitamin D in human reproduction: a narrative review. Int J ClinPract (2013) 67:225–35. doi: 10.1111/ijcp.12031.
14. Lerchbaum E, Obermayer-Pietsch B. Vitamin D and fertility: a systematic review. Eur J Endocrinol (2012) 166:765–78. doi: 10.1530/EJE-11-0984
15. Blomberg Jensen M. Vitamin D metabolism, sex hormones, and male reproductive function. Reproduction (2012) 144:135–52. doi: 10.1530/REP-12-0064.
16. He C, Lin Z, Robb SW, Ezeamama AE. Serum Vitamin D Levels and Polycystic Ovary syndrome: A Systematic Review and Meta-Analysis. Nutrients (2015) 7:4555–77. doi: 10.3390/nu7064555.
17. Chang EM, Kim YS, Won HJ, Yoon TK, Lee WS. Association between sex steroids, ovarian reserve, and vitamin D levels in healthy nonobese women. J ClinEndocrinolMetab (2014) 99:2526–32. doi: 10.1210/jc.2013-3873
18. Lundqvist J. Vitamin D as a regulator of steroidogenic enzymes. F1000Research (2014) 3:155. doi: 10.12688/f1000research.4714.1
19. Wang JH, Tuohimaa P. Regulation of 17beta-hydroxysteroid dehydrogenase type 2, type 4 and type 5 by calcitriol, LXR agonist and 5alphadihydrotestosterone in human prostate cancer cells. J Steroid BiochemMolBiol (2007) 107:100–5. doi: 10.1016/j.jsbmb.2007.02.009.
20. Lundqvist J, Norlin M, Wikvall K. 1alpha,25-Dihydroxyvitamin D3 exerts tissue-specific effects on estrogen and androgen metabolism. BiochimBiophysActa (2011) 1811:263–70. doi: 10.1016/j.bbalip.2011.01.004
21. Azadi-Yazdi M, Nadjarzadeh A, Khosravi-Boroujeni H, Salehi-Abargouei A. The Effect of Vitamin D Supplementation on the Androgenic Profile in Patients with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis of Clinical Trials. HormMetab Res (2017) 49:174–9. doi: 10.1055/s-0043-103573
22. Sova H, Unkila-Kallio L, Tiitinen A, Hippelainen M, Perheentupa A, Tinkanen H, et al. Hormone profiling, including anti-Mullerian hormone (AMH), for the diagnosis of polycystic ovary syndrome (PCOS) and characterization of PCOS phenotypes. GynecolEndocrinol (2019) 35:595–600. doi: 10.1080/09513590.2018.1559807.

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