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Vitamin D Linked to Fertility Outcomes in ART

— Only 26% of women had sufficient levels

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Adequate levels of vitamin D were associated with better fertility outcomes in women undergoing assisted reproduction treatment (ART), a meta-analysis of recent studies found.

The analysis of 11 studies including 2,700 women reported that those with adequate vitamin D were 33% more likely to achieve live birth than those with deficient or insufficient levels (OR 1.33, 95% CI 1.08-1.65), said researchers led by Justin Chu, PhD, of the University of Birmingham in the U.K.

Women with adequate vitamin D were also 34% more likely to achieve a positive pregnancy test (OR 1.34, 95% CI 1.04-1.73) and 46% more likely to achieve a clinical pregnancy (OR 1.46, 95% CI 1.05-2.02), Chu's group reported online in *Human Reproduction.*

However, the meta-analysis found no significant association between vitamin D concentrations and risk for miscarriage (OR 1.12, 95% CI 0.81-1.54), Chu and colleagues said.

Only 26% of women in the studies analyzed had sufficient levels of vitamin D (>30 ng/mL). Approximately 45% had insufficient levels (<30 ng/mL) and 35% were vitamin D deficient (<20 ng/mL), the investigators said.

"Vitamin D deficiency has been associated with an increased risk of abnormal pregnancy

implantation as well as obstetric complications such as pre-eclampsia and fetal growth restriction. However, the effect of vitamin D on conception and early pregnancy outcomes in couples undergoing ART is poorly understood," Chu's group wrote.

"Testing for vitamin D concentrations is relatively cheap and widely available, and its treatment is not costly," Chu said in a statement. "It could be that correcting vitamin D deficiency could benefit women undergoing assisted reproduction treatment, but further research is needed to test this."

"In the meantime, women who want to achieve a successful pregnancy should not rush off to their local pharmacy to buy vitamin D supplements until we know more about its effects," Chu cautioned. "It is possible to overdose on vitamin D and this can lead to too much calcium building up in the body, which can weaken bones and damage the heart and kidneys."

The meta-analysis provides strong evidence for the role of vitamin D in pregnancy outcomes, said Lauri Wright, PhD, director of the clinical nutrition program at the University of North Florida in Jacksonville, in an email to *MedPage Today.* Wright, a spokesperson for the Academy of Nutrition and Dietetics, was not involved in the study.

"We have long known the importance of vitamin D for bone health. Additional functions of vitamin D that we are learning about include its role in the immune system and preventing cancer. Recently, more and more studies have shown the importance of vitamin D for conceiving as well as having a healthy pregnancy," Wright said.

"I believe we are going to see practice guidelines to measure vitamin D levels in women trying to conceive and who are pregnant," Wright said. "And the guidelines will also include vitamin D supplementation recommendations."

The 11 studies included in the meta-analysis were published from 2010 through 2015. They were all cohort studies, six retrospective and five prospective. Sample sizes ranged from 84 to 517 women. Nine studies reported the women's ages, and, of these, seven had a mean age of approximately 37 years while two had a higher mean age of approximately 40 years.

Eight of the studies used serum measurements of vitamin D, two used both follicular fluid and serum vitamin D, and one study used follicular fluid alone. Some studies measured vitamin D before the start of ART, while others assessed vitamin D at the time of oocyte retrieval.

Previous studies have reported seasonal variation in conception rates, with higher rates in the summer and fall. "The exact mechanism behind this has not been explained," Chu and

colleagues said. "It is possible that an increase in sun exposure and greater sunlight luminosity increases the body's store of vitamin D, thereby yielding higher conception rates in summer and autumn."

Previous research has also shown that vitamin D has an impact on immunomodulation within the endometrium, reducing levels of active inflammatory cytokines. "The expression of vitamin D receptors at the level of the endometrium and the role of vitamin D in the transcription of the HOX10A gene (found to be of key importance in implantation) suggest that the immunomodulatory effects of vitamin D may have a direct impact on implantation and therefore the likelihood of reproductive treatment success," Chu's group stated.

However, it is also possible that vitamin D level is simply a marker for general good health, they said.

A potential limitation of the meta-analysis was that the cohorts of women had different characteristics and that the ART protocols also differed among the studies, Chu and colleagues said. "However, this is not necessarily a disadvantage as some degree of clinical heterogeneity can increase the generalizability of the findings to wider infertility populations," they added.

"To further investigate the value of treatment of vitamin D deficiency in the infertile population an interventional trial would be necessary," they said.

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Wright reported no conflicts of interest.

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