A biochemical view: vitamin D levels do not affect in vitro fertilization outcomes following the transfer of euploid blastocysts

TO THE EDITORS: We read with great interest the recently published article by Franasiak et al in which the authors aimed to characterize the relationship between serum 25-hydroxy vitamin D (25-OH D) levels and implantation and clinical pregnancy rates in women who undergo a euploid blastocyst embryo transfer. They concluded that vitamin D status was unrelated to pregnancy outcomes in women undergoing euploid embryo transfer. Measuring serum 25-OH D levels did not predict the likelihood that euploid blastocyst embryos will implant and these results may not apply to women who do not undergo extended embryo culture, blastocyst biopsy for comprehensive chromosome screening, and euploid embryo transfer. However, we think that there are some points that should be emphasized about this study.

First, as seen in the "Materials and Methods" section of the study by Franasiak et al, patients were selected from the electronic medical record from December 2012 through December 2013. Additionally, authors have used reference ranges, which represent clinical decision values that apply to males and females of all ages. As is known, serum 25-OH D levels are affected by many factors including pigmentation, sunlight exposure, clothing, and the season of the year. The recent study by Kasahara et al revealed that vitamin D levels peak in August and trough in February in the general population of the United States. However, we think that, especially in population-based studies, time of sampling, an important preanalytical factor due to the seasonality of serum vitamin D levels, should be considered for avoiding patient selection bias.

Second, since markedly different methods are used for vitamin D testing across clinical laboratories and reliability of these methods are controversial, the importance of a variety of measurements could be specified in the conclusion. Additionally, if available, authors should have used liquid chromatography-tandem mass spectrometry, which is a state-of-the-art analytical technique for vitamin D measurement and offers advantages of improved specificity and sensitivity.

In conclusion, preanalytical factors such as time of sampling and/or seasonality of the measure and should be considered for the studies including vitamin D measurements and use of state-of-the-art methods for vitamin D measurement would improve credibility of the study.

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REFERENCES

REPLY

We read with interest the commentary by Sertoglu et al in response to our article in which we detail the lack of correlation between 25-hydroxy vitamin D (25-OH D) levels and in vitro fertilization outcomes when embryonic aneuploidy and quality are normalized. Indeed, when using either categorical ranges for 25-OH D (<20, 20-29.9, and ≥30 ng/mL) or serum 25-OH D as a continuous variable in a receiver operating characteristic analysis, a meaningful difference was not found.

First, we agree that a study of 25-OH D’s effect on health and disease is challenging as it has been shown to be affected by many factors, including age, race, season of sampling, and body mass index. We further agree with the authors that these factors must be considered and accounted for when analyzing 25-OH D’s effects, which is why all of these factors were controlled for in the final multivariable logistic regression included in the article. Even after controlling for these factors, no difference emerged.

Second, as Sertoglu et al point out, the most appropriate analytic method for serum 25-OH D is controversial. To standardize our measurements, all samples were run in the same reference laboratory on a single analytic immunnoassay system. The serum samples, while collected over a year, were batched and run together with the same assay. The