



Vitamin D and endometriosis: Is there a correlation with disease severity?

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Dear Editor

We read with great interest the article by Baek et al. [1] entitled “Differences in 25-hydroxy vitamin D and vitamin D-binding protein concentrations according to the severity of endometriosis” that was recently published in this journal. In this observational study, the authors enrolled women affected by mild (n=9) and advanced endometriosis (n=7), as well as healthy controls (n=16), and evaluated serum 25-hydroxy vitamin D and vitamin D-binding protein concentrations according to the severity of disease [1].

It is well known that vitamin D metabolism and related cellular pathways play a crucial role in the regulation of immune response activity; the actions of vitamin D have been studied in many different biological settings, including autoimmune disease, tumors, and gynecological diseases such as endometriosis [2,3]. With regard to endometriosis, a benign chronic disease, previous studies have reported inconsistent findings regarding the relationship of vitamin D with clinical severity; notably, in the present study, the authors reported no relationship between hormone levels and the severity of endometriosis [1].

Baek et al. [1] should be congratulated for their findings and their vitally important contribution in clarifying the role of vitamin D in endometriosis, which is a controversial and complex topic. With this in

mind, we would be like to share some reflections on this study. Overall, a methodological concern may be that the authors did not precisely report whether the enrolled patients presented the same specific disease localization; in light of recent evidence, it is likely that peritoneal implants, deep-infiltrating implants, and ovarian endometriomas have some distinctive pathogenic aspects. For this reason, we suggest that the type and localization of endometriosis should be reported.

Another methodological issue is the use of the American Society for Reproductive Medicine (ASRM) classification to describe the severity of the disease. According to this classification, four stages are recognized in relation to the location, amount, depth, and size of endometriotic implants; however, this classification poorly reflects the severity of pain, other clinical symptoms, and infertility risk. Thus, although this classification is widely used in the current literature, it is considered outdated and limited in terms of its ability to describe endometriosis. Recently, new studies are being conducted to validate other classification system, such as the Enzian system; nevertheless, demand remains present for accurate new classification systems [4].

In addition, because of the small amount of cases, the authors merged stages 1–2 and 3–4 of the ASRM classification into two groups (mild and advanced endometriosis). This choice effectively creates a new subdivision, which may lead to bias in the interpretation of the study results, and at least makes it more challenging to compare their results with other studies investigating this issue.

In conclusion, the role of vitamin D in endometriosis remains to be clarified, and the value of using this hormone as a serum biomarker of the extent and severity of disease remains an open question. At the moment, there are no validated biological serum, urinary, or endometrial markers that can quantify the presence and severity of endometriosis. Moreover, it would be interesting to know whether vitamin D metabolism and related cellular pathways may be a future

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therapeutic target for this benign hormone-dependent disease [5]. Further studies are needed to draw definitive conclusions on the relationship between endometriosis and vitamin D.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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