Does the observation of lower ratio of anterior anogenital distance and posterior anogenital distance appear in adolescent and remain constant in women diagnosed with polycystic ovary syndrome?

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DEAR EDITOR,

We read the study by Simsir et al[1] published in the recent issue of the *Journal of the Chinese Medical Association* with interest. The authors pioneered to compare the difference of the anogenital distance (AGD) between women with and without polycystic ovary syndrome (PCOS) and found the larger AGD in women with PCOS compared to women without, although it is absent of statistical significance. Although using the ratio of anterior AGD and posterior AGD as the parameter, the authors found that ratio of anterior AGD and posterior AGD is good correlation with the diagnosis of women with PCOS, since they found ratio of AGD and posterior AGD is statistically significantly smaller in women with PCOS than that in women without.[1] We congratulate the success of the authors' publication, but some questions are raised and hope to see the response by authors.

First, the diagnosis of PCOS is made by criteria, and three criteria are available now, including the National Institutes of Health criteria, Rotterdam criteria, and Androgen Excess and PCOS criteria.[2] Among these, Rotterdam criteria might be most popular, since the 2018 international evidence-based guideline also commends it.[3] For women to be diagnosed with PCOS, at least two out of the following three PCOS features should be met, including clinical and/or biochemical androgen excess, oligo-ovulation or anovulation, and polycystic ovarian morphology on ultrasound.[2] We are wondering what the category can be belonged to. Did the authors consider the ratio of anterior AGD and posterior AGD as clinical androgen excess? In fact, the authors have provided the results to show the statistically significantly negative correlation between the ratio and free androgen index. However, much more evidence might be needed to clarify that this phenotype is really secondary to androgen excess.

Two recent interesting studies have evaluated the role of phenotype on the impact of the development of PCOS.[5,6] Zore et al[6] found PCOS phenotype is established in early adolescence, remains constant into adulthood, and is not related to body mass index.[6] If the ratio of anterior AGD and posterior AGD is a typical phenotype of PCOS, the lower ratio of anterior AGD and posterior AGD might be found in their early adolescence age, suggesting that early intervention or prevention strategy can be performed as early as possible. By contrast, team by Torchen et al[5] found that despite similarly elevated free T levels on girls with obesity and premenarchal daughters of women affected with PCOS, premenarchal daughters of women with PCOS had a statistically significant higher serum level of anti-müllerian hormone than girls with obesity did, suggesting that girls with obesity still lack alterations in ovarian folliculogenesis, a key reproductive features of PCOS. Then, the authors concluded that elevated testosterone level in girls of obesity might not be an early biomarker for PCOS. If free androgen index can not be used as early biomarker for PCOS, it is supposed the value of the subsequent change after elevated free androgen index, such as the ratio of anterior AGD and posterior AGD might not be a good marker for PCOS.

Finally, we are glad to read this article and hope to see more discussion about this. We are looking forward to learning the authors' kind response.

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