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Perspectives on "Assessment of hormone measurement methods in girls with premature adrenarche, polycystic ovary syndrome, and non-classical congenital adrenal hyperplasia"

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We read with interest the article by Uçar et al. entitled "Assessment of hormone measurement methods in girls with premature adrenarche, polycystic ovary syndrome, and non-classical congenital adrenal hyperplasia.".[1] Their comparison of traditional immunoassays with liquid chromatography – tandem mass spectrometry (LC-MS/MS) for measuring steroid hormones in hyperandrogenic conditions highlights an important diagnostic issue. Variability in outcomes of assay measurement can not only lead to unnecessary testing but may also delay diagnosis and affect outcomes. After carefully reviewing the methodology and results of the article, we would like to emphasize some points that may help to enhance the validity of the findings.

The authors compared immunoassay and LC-MS/MS hormone values using a Wilcoxon test. However, this approach only assesses statistical variability between methods and does not evaluate their agreement among methods or interchangeability. For a correct method-comparison analysis, Bland–Altman plots or Passing–Bablok regression are recommended. As Bland-Altman analysis measures both bias and agreement limits, it provides a more comprehensive understanding of analytical consistency compared to simple significance testing.[2] Using such approaches would enhance the reliability and comparability of future results.

Another concern arises from variable androstenedione area under the curve (AUC) values for polycystic ovary syndrome (PCOS), reported in the abstract and results. This article reports androstenedione AUC as 0.949 in the abstract and 0.792 in the results section. Such variability suggests potential reporting or analytical error, producing confusion among the readers and raising concerns about data accuracy. Cross-checking data consistency across sections before publication would help in this regard. Another concern is the lack of information on standardized sampling conditions for hormone measurements; the study does not clarify whether measured factors were standardized or controlled during sample collection. Steroid hormone concentrations can vary with factors such as time of day, fasting, menstrual cycle, and pubertal stage.[3] In analytical endocrinology, such uncontrolled variability can not only imitate or exaggerate differences between assay methods but also affect diagnostic interpretation and compromise the validity of findings. Clarifying sampling procedures would therefore improve reproducibility and interpretability.

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Another relevant aspect relates to the authors' claim that electrochemiluminescence Immunoassay (ECLIA)-measured dehydroepiandrosterone sulfate (DHEAS) showed higher diagnostic performance for premature adrenarche. This overlooks the known tendency of immunoassays to overestimate DHEAS due to cross-reactivity with other sulfated steroids.[4] This means higher sensitivity might represent false positives rather than true accuracy. Future studies should confirm DHEAS results with LC-MS/MS and use method-specific reference ranges and confirmatory tests to improve diagnostic precision.

Overall, the efforts of the authors significantly contribute to pediatric endocrinology by addressing a major analytical problem. However, ensuring statistical agreement, data consistency, and control of pre-analytical variability will strengthen validity and applicability of findings to medical practice. Using robust analytical tools and LC-MS/MS confirmation would improve diagnostic reliability, prevent misinterpretation, and ensure medical decisions for diagnosis and prognosis depend on accurate and standardized hormone measurements.

Author contribution

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Conflict of interest

The authors declare that there is no conflict of interest.

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