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Sensitivity, Specificity, and Predictive Value of Urinary Androgen Metabolites for the Diagnosis of Polycystic Ovary Syndrome

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Objective

The objective of this study was to determine if urinary androgen metabolite concentrations measured using an at-home dried urine sampling method and an accompanying gas chromatography-tandem mass spectrometry (GC-MS/MS) assay could be used to confirm or rule out polycystic ovary syndrome (PCOS).

Materials and Methods

This was a retrospective observational cohort study conducted using a database containing 144,561 laboratory accessions that were submitted between January 1, 2016 and December 9, 2019 by 129,883 patients. These patients collected urine samples on filter paper at home and sent the collections to the laboratory to be processed. Urinary concentrations of androsterone, dehydroepiandrosterone sulfate (DHEA-S), epitestosterone, etiocholanolone, testosterone, 5α-androstanediol, 5β-androstanediol, and 5α-dihydrotestosterone (DHT) were measured. The database included a total of 2050 patients with a reported diagnosis of PCOS and 27488 patients who did not report a PCOS diagnosis. A "urinary androgen index" was created comprising all measured androgen metabolites. Mixed models were then created to determine sensitivity, specificity, and predictive values of the components of this urinary androgen index.

Results

Mixed models determined that for patients with a measured urinary androgen index greater than or equal to 4 (4 or more androgen metabolites above the reference range) the sensitivity was 0.44, the specificity was 0.78, the positive predictive value was 0.13, and the negative predictive value was 0.95. For patients with a measured epitestosterone, etiocholanolone, or testosterone above the reference range the sensitivity was 0.70, the specificity was 0.53, the positive predictive value was 0.10, and the negative predictive value was 0.96. For patients with a measured urinary testosterone higher than the 75th percentile of the reference range, the sensitivity was 0.47, the specificity was 0.76, the positive predictive value was 0.13, and the negative predictive value was 0.95.

Urinary Androgen Index

"Urinary Androgen Index" (4+ androgens higher than the upper reference range)	PCOS Diagnosis?		
	Report PCOS	No PCOS	All Patients
4 or more higher than upper reference range	906	5944	6850
3 or fewer higher than the upper reference range	1144	21544	22688
	2050	27488	2050/29538 = 6.9% Study Prevalence

Sensitivity	0.44 (44%)
Specificity	0.78 (78%)
Positive Predictive Value	0.13 (13%)
Negative Predictive Value	0.95 (95%)

Urinary Androgens Measured

- Androsterone
- Dehydroepiandrosterone sulfate (DHEA-S)
- Epitestosterone
- Etiocholanolone
- Testosterone
- 5α-androstanediol
- 5β-androstanediol
- 5α-dihydrotestosterone (DHT)

Etiocholanolone, Testosterone, and Epitestosterone

Either Etiocholanolone, Testosterone, or Epitestosterone higher than the upper reference range	Report PCOS	No PCOS	All Patients
Yes	1445	12783	14228
No	605	14705	15310
	2050	27488	

Sensitivity	0.70 (70%)
Specificity	0.53 (53%)
Positive Predictive Value	0.10 (10%)
Negative Predictive Value	0.96 (96%)

Testosterone Only

Testosterone higher than the 75th percentile	Report PCOS	No PCOS	All Patients
Yes	963	6628	7591
No	1087	20860	21947
	2050	27488	

Sensitivity	0.47 (47%)
Specificity	0.76 (76%)
Positive Predictive Value	0.13 (13%)
Negative Predictive Value	0.95 (95%)

Conclusions

Urinary androgen metabolites measured using a dried urine sample and a validated GC-MS/MS assay demonstrated low positive predictive values, but high negative predictive values for PCOS suggesting that these measures may be of use in ruling out PCOS.

Impact Statement

In this large general population study, a dried urine sampling method measuring androgen metabolites demonstrated the potential to be effective at ruling out PCOS. This method may represent a new, convenient, at-home, non-invasive tool for clinicians and researchers to use in settings where barriers exist to in-person patient evaluation or ultrasonography. When combined with additional information available from urine sampling, this tool may provide a comprehensive panel of results to inform both clinical investigation and decision making.