

Comparison of Cyclic Urinary Estrogen and Progesterone Metabolite Patterns Between Women Reporting Menses and Women Reporting No Menses

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Objective

To determine if monthly urinary patterns of estrogen and progesterone, collected as dried urine samples and measured with a GC-MS/MS assay, differ between women who reported menses and women who reported no menses.

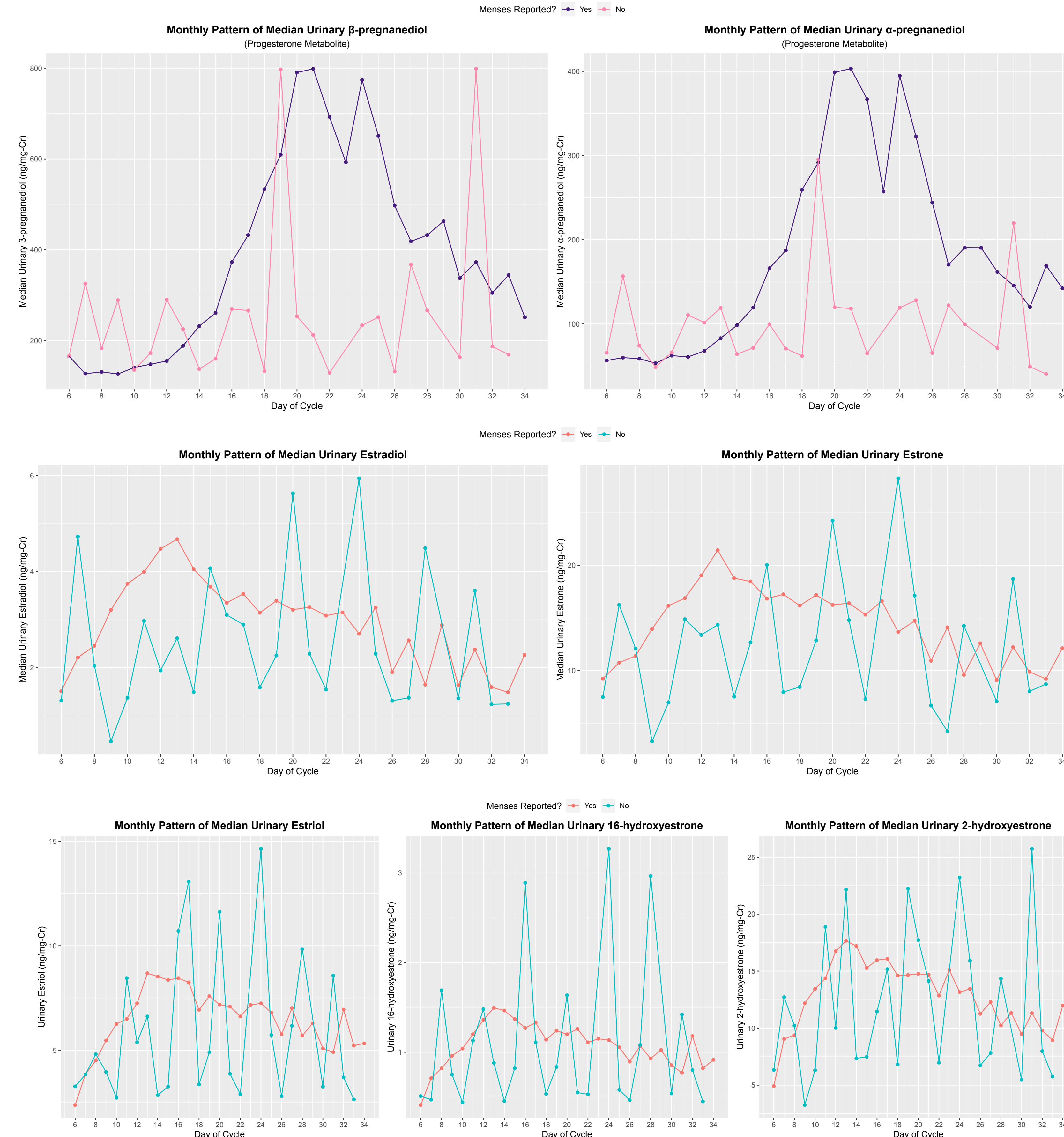
Materials and Methods

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 individuals. From this database, 1604 individuals completed a cycle collection and met inclusion criteria for the study (female sex, age between 17 and 50 years, body mass index [BMI] between 16 and 55 kg/m², and urinary creatinine > 0.1 ng/mL). Progesterone was measured as its urinary metabolites 5 α -pregnane-3 α , 20 α -diol (α -pregnanediol) and 5 β -pregnane-3 α , 20 α -diol (β -pregnanediol), with total pregnanediols calculated as α -pregnanediol plus β -pregnanediol. Estrogen was also measured via the urinary metabolites with total estrogens calculated as the sum of all 10 measured metabolites. Mixed models to account for repeated measures were used to compare urinary estrogen and progesterone patterns between women who reported menses and women who reported no menses.

Results

Of the 1604 patients included in the study, 93% (1494) reported menses and 7% (110) reported no menses. The mean age (\pm SD) was 36.2 \pm 7.1 for the group reporting menses and 34.9 \pm 9.6 for the group reporting no menses. The mean BMI was 24.2 \pm 4.6 for the group reporting menses and 24.6 \pm 6.0 for the group reporting no menses. No statistically significant difference existed between either the mean age ($p = 0.15$) or BMI ($p = 0.43$). A mixed model showed that reporting vs. not reporting menses had an effect on the trajectories of pregnanediols that was highly significant ($p < 0.0001$) with an overall effect of increasing total pregnanediols an average of 246.9 (46.2) ng/mg-Cr/day. The model also showed that the observed pregnanediol patterns between the two groups of women (menses vs. no menses) were significantly different ($p < 0.0001$). Similarly, women reporting menses had a significantly different trajectory of total estrogens than women reporting no menses (Average effect: $\Delta = 18.1 \pm 5.0$ ng/mg-Cr/d; $p < 0.0001$). The individual estrogen metabolites, including estradiol, showed similar findings when analyzed separately.

Progesterone & Estrogen Metabolite Patterns



Subject Characteristics

| Variable | Total | Reported Menses | No Menses | p value |
|--|------------------------|------------------------|----------------------|---------|
| Age (years) | 36.1 \pm 7.3 | 36.2 \pm 7.1 | 34.9 \pm 9.6 | 0.15 |
| BMI (kg/m ²) | 24.2 \pm 4.7 | 24.2 \pm 4.6 | 24.6 \pm 6.0 | 0.43 |
| Peak α -pregnanediol (ng/mg-Cr) | 560.4 (318.1, 882.8) | 576.8 (346.7, 899.3) | 111.2 (65.4, 553.5) | <0.0001 |
| Peak β -pregnanediol (ng/mg-Cr) | 1102.2 (678.0, 1606.0) | 1131.9 (737.1, 1628.6) | 305.5 (156.1, 991.1) | <0.0001 |

*Mean \pm standard deviation for normally distributed variables; Median (IQR) for variables with a skewed distribution.

Conclusions

The method used in this study effectively captured the expected estrogen and progesterone patterns in women who reported menses. Additionally, there were clear and significant differences in these patterns between women who reported menses and women who reported no menses.

Impact Statement

This convenient, at-home collection method and the accompanying validated assay represents a tool that may be useful in a variety of clinical and research settings as it decreases the need for office visits and staff to perform collections needed to evaluate estrogen and progesterone patterns over the course of a menstrual cycle.

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