BACKGROUND & HYPOTHESES

How much do ovarian hormone levels vary from cycle to cycle?

Many studies assume low variation (i.e., high reliability) of ovarian steroid levels among a woman’s ovarian cycle, but this assumption may not be justified. The few relevant studies have reported low1,2 and high5 inter-cycle variation in hormone levels. Ovarian hormone levels vary with energy intake and expenditure1 and lactation status,1,2,3 but other than a study of 22 rural Polish women,4 there has been little evaluation of the magnitude of the contribution of these factors to natural inter-cycle hormone variation. In addition, the question of whether seasonal energetic stress affects only anovulation rates or also reduces hormone levels in ovulatory cycles per se has not been examined.

We tested 3 hypotheses regarding the extent and sources of progesterone (P) variation within and between individuals in a large sample of breastfeeding and non-breastfeeding Bolivians followed through the agricultural cycle in a single year.

HYPOTHESES:

Null Hypothesis 1: P levels in a woman’s ovulatory cycles are not correlated. 
Alternative Hypotheses: P levels in a woman’s ovulatory cycles are significantly:
  1a: ... but only modestly correlated.
  1b: ... and highly correlated.

Null Hypothesis 2: P levels in ovulatory cycles do not vary with seasonal variation in energy intake and expenditure.

Alternative Hypothesis 2: Energetically stressful seasons are significantly associated with reduced P levels in ovulatory cycles.

Null Hypothesis 3: Among cycling women, breastfeeding status does not contribute to inter-woman variation in P levels in ovulatory cycles.

Alternative Hypothesis 3: Among cycling women, breastfeeding status is significantly associated with variation in P levels in ovulatory cycles.

STUDY DESIGN & METHODS

Study Population. Participants (n=316 women) in Project REPA, a longitudinal study of health and reproduction in rural agropastoral communities in Bolivia (4000m altitude).

Data Collection. Menstruating women (n=191; 98 breastfeeding, 93 not breastfeeding) were visited every other day by a bilingual (Spanish/Aymara) promoter who recorded menstrual bleeding and lactation status, and collected a saliva sample later assayed for progesterone (P).4,10

Ascribing Ovulation. Progesterone levels are exceedingly low in anovulatory cycles. Inclusion of these cycles in analyses unaccountably obscures the issue of whether inter-cycle hormonal variation is principally a consequence of anovulation (i.e., hormone levels in ovulatory cycles of a given woman are highly correlated) or of anovulation plus significant hormonal variation in a woman’s ovulatory cycles. We distinguished anovulatory cycles using previously described methods.4,10

Statistical Analyses (using SPSS v29.0) included only ovulatory cycles (n=392 cycles, 122 women).

The dependent variable, mean peak-luteal-P, was defined as (the area-under-the-curve bounded by ±2.5 days from the day of maximum observed P)/5 days.

Predictor variables. Season: early harvesting and planting (shaded grey in Fig 1) are the most energetically demanding periods (“poor”), others being relatively less arduous (“good”).

Breastfeeding status: Classes were classified as “breastfeeding” or “not breastfeeding” based on women’s recorded practices. Woman’s age was based on several cross-verified sources.

RESULTS

Null Hypothesis 1: Rejected. Mean peak-P levels in an individual’s ovulatory cycles are correlated (Figures 5 and 6, Table 1). Alternate Hypothesis 1a: Supported. These mean peak-P levels are only modestly correlated. Alternate Hypothesis 1b is not supported.

Alternate Hypothesis 2: Supported. Mean peak-P levels in ovulatory cycles are significantly lower in the poor season (Figure 7, Table 2). However, seasonality accounted for only 4% of the total variation in mean peak-P, indicating that the source of most of the hormonal variation is unexplained.

Null Hypothesis 3: NOT Rejected. (i.e., alternate hypothesis 3 was NOT supported). Breastfeeding status does not contribute to inter-woman variation in P levels in ovulatory cycles. (Figure 7, Table 2).

CONCLUSIONS

- High levels of both intra- and inter-woman variation - ICC = 0.32. The intra-class correlation coefficient (ICC) is defined as the ratio of the between-subject variance divided by the total variance in the sample. Thus, 68% of the total variation in our sample is due to intra-woman variation.

- Seasonality significantly influences mean luteal peak progesterone levels.

- Mean peak-P levels higher in Good seasons.

- But, not the only factor, explains only 4% of the variance (p < 0.001).

- Breastfeeding status was not significantly related to inter-woman variation in mean-luteal peak progesterone levels.

- Findings are surprising, given our expectations based on physiological understandings of lactation and suppression of reproductive hormones.

- Future analyses will account for other important factors that mediate the impact of breastfeeding on progesterone levels.

- Age of child being breastfed

- Younger toddlers and infants tend to consume more breast milk than older toddlers.7,8

- Age and anthropometrics of the mother; either of these variables might mediate maternal hormonal response to breast feeding.

- Despite concluding that seasonality significantly influences mean luteal peak P levels, high levels of variation remain unexplained.

- This variation has major implications for both clinical and field studies.

- Our results challenge the notion of a simple “baseline” hormone level for a given woman, as P levels across cycles were only moderately correlated.

WORKS CITED


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