COMPARISON OF HOME PREGNANCY TEST WITH WEEKS ESTIMATOR AND ULTRASOUND CROWN RUMP MEASUREMENT TO PREDICT DELIVERY DATE

Sarah Johnson, PhD[1] and Sonya Godbert, CStat[1].

[1]SPD Development Company Ltd, Priory Business Park Bedford, Bedfordshire, United Kingdom, MK44 3UP.

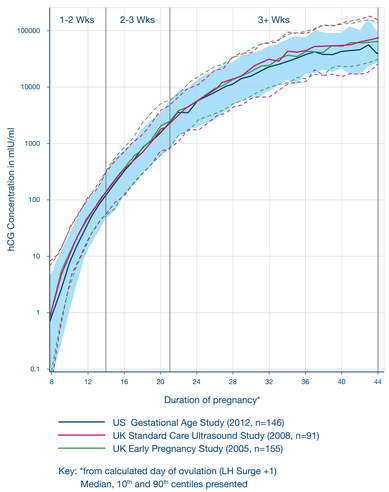
Introduction

- Women who get a positive pregnancy test result wish to know quickly how far along they are.
- Allows a woman to plan and understand her pregnancy
- Clinically important to ensure appropriate care
- An improvement on LMP is long overdue
  - Often no better than a guess, up to 70% of women don't know their LMP
  - Even if known, assumes ovulation on day 14 – a recent study found that **for half of women**, LMP provided a GA that was **5 or more days incorrect** (up to 57 days out in one case)[1]
- A new urine pregnancy test, Clearblue® Advanced Pregnancy Test with Weeks Estimator (CAPT), is available in the USA, which as well as determining pregnancy status also estimates the number of weeks since ovulation for women testing pregnant.

Test Background

The new test is a conventional digital pregnancy test that also estimates the number of weeks since ovulation. Results are displayed on an LCD as 1-2, 2-3 and 3+ weeks categories if a "Pregnant" result is returned. The basis of the weeks categorisation are the threshold level of urinary hCG that relate to the boundaries between weeks, as shown in figure 1 below, which has been demonstrated as an accurate measure of early pregnancy duration.[2]

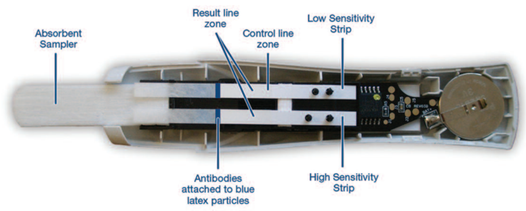
Figure 1: Plot of Median and 10th-90th centile levels of urinary hCG from 3 independent studies, with weeks categories overlain to show the derivation of thresholds relating to weeks boundaries.



Key: *from calculated day of ovulation (LH Surge +1)
Median, 10th and 90th centiles presented

Due to the exponential increase in hCG in early pregnancy[3], the test must be capable of measuring the low and high boundary levels of hCG with precision. A single lateral flow immunoassay strip is not normally able to measure across a wide concentration range with precision, therefore, this test consists of two immunoassay strips (one low and one high sensitivity) to accommodate the required range. An optical detection system and microprocessor convert the assay signal in to easy to understand results on an LCD screen. The internal architecture of this test is shown in figure 2.

Figure 2: Internal architecture of CAPT



A prospective study has found the "weeks estimator" to be 93% in agreement with time since ovulation (by LH surge)[4] and 97% in agreement with gestational age by later Crown Rump Length (CRL) Measurement at 10^{+0}-13^{+6} weeks[5].

OBJECTIVE

The objective of this study was to compare prediction of final delivery date by CAPT in comparison to ultrasound.

Methods

Data from volunteers with singleton pregnancies and a natural delivery (n=46) from the standard-of-care ultrasound study (UK)[1] and the Gestational age study (US)[2], were analysed. Both of these studies required volunteers to collect daily urine samples from preconception LMP until approximately 8 weeks GA (GA, equivalent to 6 weeks post ovulation), and had CRL recorded. A random sample of urine samples were tested using Clearblue Advanced Pregnancy Test with Weeks Estimator. Randomisation was conducted to allow equal representation per volunteer and per week of pregnancy (1-4 weeks since ovulation). Urine samples were tested in laboratory using the device (n=458 devices). The device results were used to determine the duration of pregnancy (from ovulation) on delivery day, with a "1-2" CAPT result classed as being 14 days pregnancy duration on the day of measurement, "2-3" as 21 days, and "3+" as 28 days. For comparison purposes, the duration of pregnancy from ovulation (GA-14 days) to delivery day was also calculated using CRL measurement and LMP. CRL was converted to GA using the Robinson's[6] formula. To align results, 14 days were subtracted from both CRL and LMP derived GA estimates.

Results

The demographics and menstrual cycle characteristics of the study population are summarised below:

- Mean age of volunteers was 30.48 years (range 23-41, median 30.5, SD 4.1)
- Highest education level was; 26.1% High School, 50% College/Graduate School, 23.9% Post Graduate
- Mean length of time trying to conceive was 5.8 months (range 0-48, median 4.0, SD 7.36)
- Self-reported average menstrual cycle length was a mean of 28.8 days (range 25-37, median 28.0, SD 2.58)
- Shortest self-reported cycle in the past 6 months was a mean of 26.8 days (range 10-36, median 28.0, SD 4.26)
- Longest self-reported cycle in the past 6 months was a mean of 31.5 days (range 26-60, median 30, SD 5.15)
- Mean CRL at scan was 58.6mm (range 24.5-95, median 57.5, SD 14.7) which provided a range of gestational age at time of scan of a mean of 12.5 weeks (range 9.7-20.9, median 12.3, SD 1.6)

The mean time from each volunteer's majority device results (time since ovulation) to delivery was 37.47 weeks (SD 1.52), 95% Confidence Interval 37.02-37.92, range 33.07-39.91. The mean time from ovulation to delivery based on CRL measurement was 37.40 (SD 1.75), 95% Confidence Interval 36.88-37.92, range 33-41.57. The results are outlined in Table 1.

Table 1: Summary of duration of pregnancy at delivery by using Clearblue Advanced pregnancy test (CAPT) with weeks estimator, and ultrasound to define pregnancy duration.

Duration of Pregnancy at Delivery Date (weeks, since ovulation)	n	Mean	SD	Median	5th	95th	Minimum	Maximum	Total range of variation (weeks)
By Individual CAPT Device Results	444*	37.16	1.57	37.29	34.43	39.57	32.71	40.71	8
By CAPT Device results per volunteer**	46	37.47	1.52	37.58	34.84	39.60	33.07	39.91	6.84
By CRL converted to GA by Robinson's	46	37.40	1.75	37.43	34.57	40.14	33.00	41.57	8.57
From LMP (includes approx. 2 weeks pre-ovulation)	46	37.65	2.20	37.43	34.71	39.86	32.86	47.71	14.85

*458 devices tested, 14 Not Pregnant results obtained as tested before day of expected period

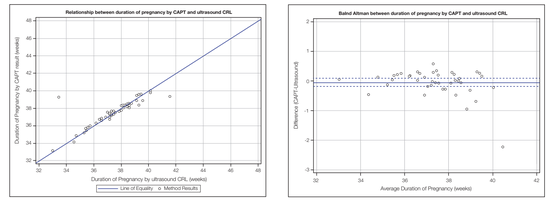
**majority decision by all tests on all samples per volunteer

The least variation in pregnancy duration at delivery was using the majority decision from all devices tested on an individual, and individual device results. Variation was slightly greater by ultrasound, and considerably greater by LMP, indicating that LMP is a poor reference of pregnancy duration.

The relationships between duration of pregnancy by CAPT compared to ultrasound (a), CAPT compared to LMP (b) and ultrasound compared to LMP (c) are shown in figure 3, with correlation coefficient calculated for each method comparison. Correlation was calculated with two volunteers (1174 and 1054) excluded from the analysis.

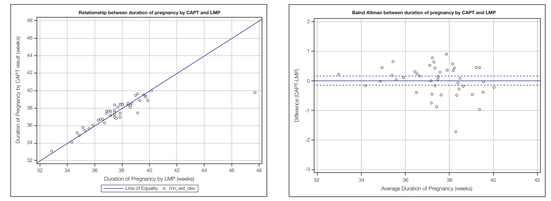
Figure 3: Relationship between duration of pregnancy assessed by CAPT, ultrasound CRL and LMP.

A: Correlation is 0.964

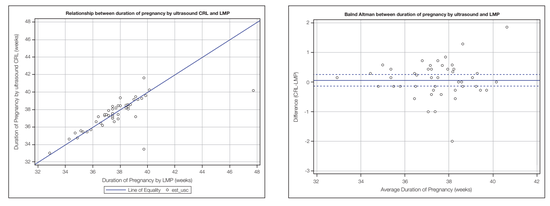


The volunteer, with duration of pregnancy 33.4 weeks by scan and 39.3 weeks by device is likely to have inaccurate scan rather than device results, as she delivered a 6lb 10oz boy.

B: Correlation is 0.947



C: Correlation is 0.924



CONCLUSIONS

- Both CAPT results and CRL methods provided comparable predictions of delivery date, with a slightly broader range seen using CRL measurement.
- The mean duration of time from ovulation to delivery was consistent with the typically reported 38 weeks.
- Range of delivery by LMP was considerably more than by other methods, indicating that it is an inaccurate measure.
- There was excellent correlation between all methods, with the highest level seen between CAPT and CRL, and the lowest between CRL and LMP.
- The new pregnancy test's "weeks estimator" provides results that much more accurate than LMP. The device results are also comparable to those of ultrasound, but are obtained earlier in pregnancy. Therefore the new device provides a woman useful and accurate information at the time of first discovering she is pregnant.

REFERENCES:

1. Johnson et al (2011) Curr Med Res Opin 27:393-401
2. Larsen et al (2013) IJGO doi:10.1016/j.ijgo.2013.05.028
3. Johnson et al (2009) Curr Med Res Opin 25:741-748
4. Johnson et al (2013) Clin Chem S209;B45
5. Johnson et al (2013) Human Reproduction 28:i5;O-012. Agreement for all device results with Crown Rump Length at 10-13+6 weeks GA was 97%, agreement by weeks category varied from 45-99% according to whether ultrasound bias and variability were accommodated.
6. Robinson et al (1975) BJOG 82:720-10

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