Code: PUB-0147
Print Date: 26-Aug-2016
Rev: 1
Status: Current
Effective Date: 23-Jun-2016
Document valid for submission purposes

Urinary human chorionic gonadotrophin (hCG) levels in early pregnancies correlate with serum hCG and may be used for the monitoring of early pregnancy well-being

S. Johnson[1], J. Shillito[2], N. Simpson[2], J. Walker[2]

H16-0497

[1]SPD Development Company Ltd, Bedford, United Kingdom.
[2]University of Leeds Teaching Hospital, Department of Obstetrics, Leeds, United Kingdom.

Background:

- Quantitative assessment of serum hCG levels represents the gold standard for the monitoring of early pregnancy
- However, this analysis is currently performed in diagnostic laboratories rather than at the point of care
- Furthermore, repeated blood tests can be inconvenient for patients who require regular monitoring of serum hCG for suspected ectopic pregnancy, miscarriage or pregnancy of unknown location
- Although qualitative urinary hCG tests represent a common and convenient tool for the diagnosis of pregnancy, it remains unclear whether quantitative assessment of urinary hCG could be used for the monitoring of early pregnancy well-being

Study Objectives:

- Track urinary hCG levels in early pregnancy from viable, ectopic and miscarried pregnancies
- Correlate hCG urine and serum levels
- Evaluate the validity of using urinary hCG rise and fall for monitoring of early pregnancy well-being

Methods:

- This was an observational cohort study
- **Study population:** Women attending the early pregnancy unit of St. James's Hospital, Leeds, with either a previous history of miscarriage / ectopic pregnancy (cohort A) or a suspected miscarriage / ectopic pregnancy (cohort B)
  - Participants were divided into three groups based on pregnancy outcomes: viable pregnancies, miscarriages and ectopic pregnancies
  - Monitoring of urinary and serum hCG levels started on the day of referral and continued until the 12th week of pregnancy (gestational age determined by the date of the last menstrual period [LMP]) for viable pregnancies and until resolution of an ectopic pregnancy / miscarriage in other participants
- **Analysis of hCG levels:** Urinary hCG levels were measured in the first morning urine samples using AutoDELFIA®, and serum hCG levels were measured using an automated immunoassay system
  - Urine creatinine was measured to correct for urine concentration

Results:

- A total of 82 participants were enrolled on the study (participant demographics are outlined in Table 1)
- Overall, 50 participants completed the study, 20 were withdrawn early, 8 left the study and 4 were lost to follow-up

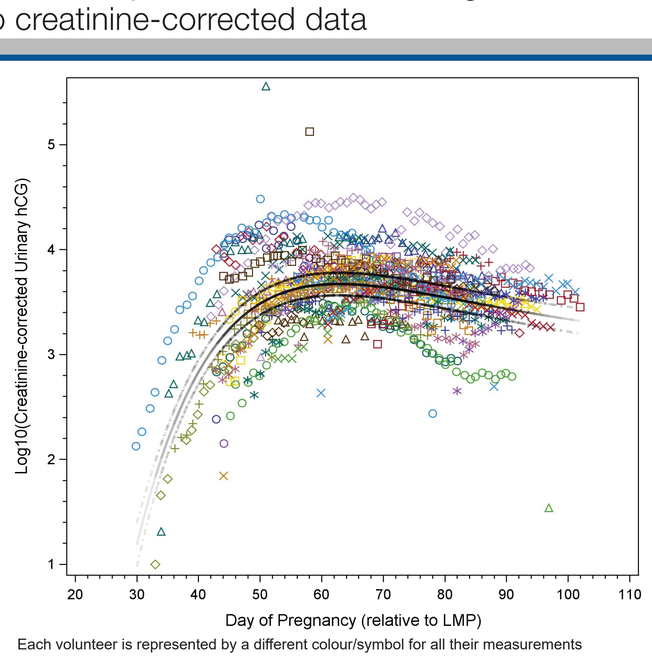
Table 1. Participant demographics

Variable	Viable pregnancy	Miscarriage	Ectopic pregnancy	Inconclusive/missing	Total
All, n (%)	49 (60)	17 (21)	11 (13)	5 (6)	82 (100)
Cohort A, n (%)	44 (90)	9 (53)	0	2 (40)	55 (67)
Cohort B, n (%)	5 (10)	8 (47)	11 (100)	3 (60)	27 (33)
Age, n (%)					
18–25 years	11 (22)	6 (35)	2 (18)	2 (40)	21 (26)
26–30 years	14 (29)	3 (18)	2 (18)	1 (20)	20 (24)
31–35 years	16 (33)	2 (12)	4 (36)	1 (20)	23 (28)
36–40 years	5 (10)	5 (29)	3 (27)	1 (20)	14 (17)
41–45 years	3 (6)	1 (6)	0 (0)	0 (0)	4 (5)
Previous live births, n (%)					
0	21 (43)	6 (35)	6 (55)	2 (40)*	35 (43)*
1–2	25 (51)	10 (59)	4 (36)	1 (20)	40 (49)
3–5	3 (6)	1 (6)	1 (9)	0 (0)	5 (6)
Previous miscarriages, n (%)					
0	13 (27)	7 (41)	6 (55)	2 (40)*	28 (34)*
1–2	25 (51)	7 (41)	5 (45)	1 (20)	38 (46)
3–4	8 (16)	2 (12)	0 (0)	0 (0)	10 (12)
4–8	3 (6)	1 (6)	0 (0)	0 (0)	4 (5)

*Information missing for two participants

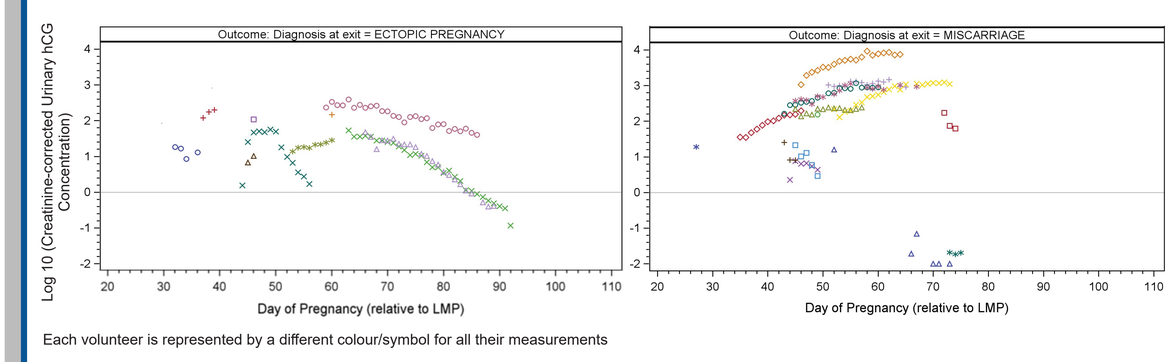
- Viable pregnancy profiles were best modelled by the critical exponential model (Figure 1)
- Within-subject variability was reduced by 58.7% after correcting for creatinine; thus, the results shown relate to creatinine-corrected data

Figure 1. Plot of creatinine-corrected urinary hCG (mIU/ml; log transformation) by day of pregnancy (relative to LMP), overlaid with predicted values and 95% confidence intervals, using a critical exponential model



Each volunteer is represented by a different colour/symbol for all their measurements

- Miscarriage and ectopic pregnancy urinary hCG profiles did not fit well with any model, but appeared different to viable pregnancies
  - The study did not include a sufficient number of participants with miscarriage and ectopic pregnancy, and there were indications of inadequate timing and frequency of data collection in these participants; collectively, this was likely to affect the performance of the models used to characterise urinary hCG profiles in these clinical scenarios
- Time profiles of log urinary hCG concentrations for ectopic and miscarriage pregnancies are shown in Figure 2
  - Specifically, urinary hCG had a very similar time profile in participants with viable pregnancies, but differed substantially in those with ectopic pregnancies and miscarriages depending on the type and timing of the pregnancy outcome

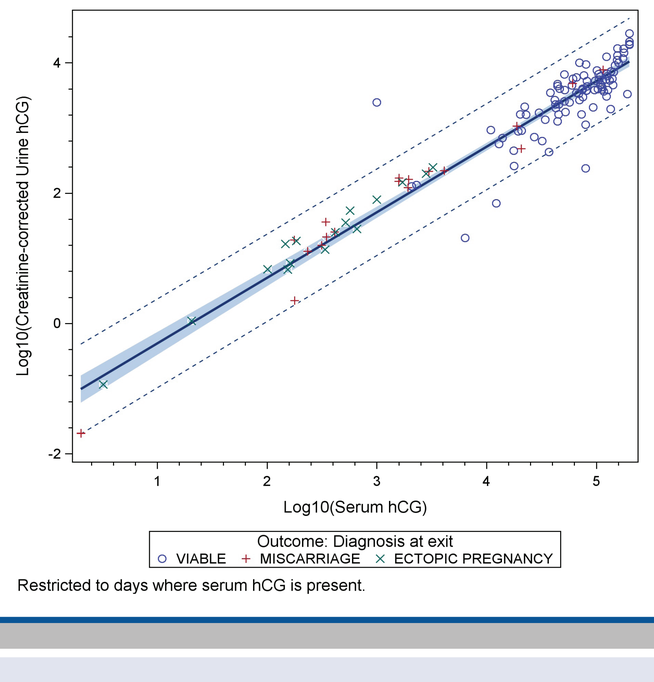


Each volunteer is represented by a different colour/symbol for all their measurements

Figure 2. Plots of creatinine-corrected log10 urinary hCG concentrations by day of pregnancy for viable pregnancies, miscarriages and ectopic pregnancies

- The study demonstrated a clear linear relationship between log urinary and log serum hCG levels that was common for all pregnancy outcomes (Figure 3)
  - The slope between the two was estimated to be 1.006 with a correlation of 0.923

Figure 3. Correlation between serum and creatinine-corrected urinary hCG (simple effects model: common intercept and slope for pregnancy outcomes overlaid with 95% confidence interval and predictions interval)



Restricted to days where serum hCG is present.

Conclusion:

- A linear relationship between log urinary and log serum hCG levels with high level of correlation was seen for all pregnancy outcomes, indicating that urinary levels provide a good reflection of serum hCG
- The possibility to model urinary hCG profiles in viable pregnancies opens new possibilities for the use of quantitative urinary hCG testing to differentiate between normal and compromised pregnancy development as an alternative to serum hCG testing

Study funding/competing interest(s):

The study was funded by SPD Development Company (Bedford, UK), a fully owned subsidiary of SPD Swiss Precision Diagnostics (Geneva, Switzerland). SJ is an employee of SPD Development Company.

Acknowledgements:

Statistical analysis conducted by B. C. Bond and K. M. Tomlinson of Prism Training & Consultancy Ltd, http://www.prismtc.co.uk

Trial registration number:

N/A

UNIVERSITY OF LEEDS

Clearblue®