

# Association Between Twin Discordance at 6–9 Weeks' of Gestation and Birthweight Complications

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Twins achieved through in-vitro fertilisation often undergo a viability ultrasound at 6–9 weeks of gestation. The presence of inter-twin crown-rump length discordance at this stage is not an uncommon finding; however the clinical significance of this is unknown. We analyzed 218 dichorionic twin pregnancies, producing two live fetuses > 24 weeks gestation, to determine whether inter-twin discordance ( $\geq$  85th centile) in the mid-first trimester was associated with birthweight discordance ( $>$  20%), or small for gestational age ( $<$  10th centile). The incidence of birthweight discordance and small for gestational age infants were determined, with no increased risk found for the discordant population. This may provide some reassurance to treating clinicians.

**Keywords:** twins, discordance, crown–rump length, first trimester, birthweight

Over the past two decades the prevalence of twin births has dramatically increased in the developed world, an increase largely attributable to the use of sub-fertility agents and in vitro fertilisation (IVF) (Eriksson & Fellman, 2007; Fellman & Eriksson, 2005). This is of concern as twins account for a disproportionate share of perinatal complications. In particular, low birthweight and twin birthweight discordance are associated with an increased risk of perinatal morbidity and mortality (Blickstein & Keith, 2004; Cooperstock et al., 2000; Demissie et al., 2002; Hollier et al., 1999).

Recently studies have focused on the first trimester to find early pregnancy indicators for birthweight discordance. Such an indicator is the presence of inter-twin crown rump length (CRL) discordance. Kalish et al. (2003) showed that a CRL discordance of  $>$  90th percentile at 11–14 weeks of gestation in 130 dichorionic pregnancies was associated with an increased risk of birthweight discordance. Similarly Tai et al. (2007) showed an association between a CRL discordance of  $>$  85th percentile at 7–14 weeks of gestation with birth-

weight discordance and adverse perinatal outcomes in 178 twins regardless of chorionicity.

Whether CRL discordance earlier in the first trimester is associated with birthweight complications has not been specifically investigated in a large cohort. This is of direct clinical relevance since IVF practitioners commonly refer women for their first ultrasound in the middle of the first trimester to confirm viability. We therefore set out to determine whether twin CRL discordance at 6 (+0 days) to 8 (+6 days) weeks of gestation is associated with small for gestational age (SGA) infants, or birthweight discordance.

## Methods

### Participants

A retrospective cohort study was performed where we identified women who conceived dichorionic twins with the assistance of IVF, and had an ultrasound at our centre at 6 (+0d) to 8 (+6d) weeks of gestation between May 2001 and June 2006. As our objective related to the birth outcomes of viable pregnancies we only included pregnancies resulting in live twins born  $\geq$  24 weeks' of gestation or greater with no evidence of genetic or congenital abnormalities. We calculated gestational age from known IVF conception dates (date of egg collection is day 14 of gestation), and therefore only included twins conceived after a fresh embryo transfer cycle.

### Definition of CRL Discordance

Six-to-nine week ultrasounds were performed by experienced obstetric ultrasonographers and CRL length measurements in millimetres were obtained. The inter-twin CRL difference was calculated with the following equation, and expressed as a percentage: (larger twin

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CRL-smaller twin CRL/ larger twin CRL)  $\times$  100. We used an 85th percentile cut-off, as defined by Tai et al. (2007), meaning the 15% of twin pairs who were most discordant were compared to the remaining cohort. We also performed subanalyses' using two other cut-offs (75th and 90th centiles).

#### Clinical Outcomes

In Australia, all IVF units are mandated to collect and report data on birth outcomes. We used this database to obtain baseline demographics and to characterise final outcomes. The primary outcomes investigated were incidences of SGA at delivery of either twin (< 10th centile for gestational age, calculated from locally derived population centile charts) (Roberts & Lancaster, 1999), and birthweight discordance (> 20% difference in birthweight).

#### Data Analysis

Unpaired student's *t* test was used to compare the two groups with continuous variables that were normally distributed. For continuous variables not normally distributed, groups were compared with the Mann-Whitney U test. Categorical variables were compared with a chi-squared test. Nonparametric data were expressed as median and 25th–75th centiles, while parametric data was expressed as the mean ( $\pm$  standard deviation).

#### Ethics Approval

Ethics approval was obtained prior to commencing our study (Project 05063, Monash Surgical Private Human Research Ethics Committee, Clayton Victoria, Australia).

## Results

We identified 218 dichorionic twin pregnancies that met our inclusion criteria. Using the 85th centile cut-off, we categorized 32 (15%) twin pregnancies into the discordant group, with 186 twin pregnancies as controls. There were no significant differences among the baseline characteristics between the two groups (Table 1). Both groups underwent an average of three treatment cycles ( $p = .99$ ) with the transfer of two embryos ( $p = .19$ ) predominating. Twins tended to be delivered at 36 weeks gestation in both the discordant and non-discordant population ( $p = .40$ ) to mothers of a similar age, being 33.4 yrs and 33.5 yrs respectively ( $p = .93$ ). Using the 85% centile cut-off, the absolute degree of discordance among our discordant population was 22.3%.

The birthweight outcomes under investigation can be seen in table 2, where mean ( $\pm$  std dev) birthweight in the CRL discordant group was 2625gms ( $\pm 392$ ), not significantly different to that seen among the nondiscordant group (2442gms ( $\pm 542$ );  $p = .07$ ). Incidence of birthweight discordance (> 20%) were also similar between the two groups (18.8% cases vs. 17.7% controls;  $p = .89$ ). The incidence of SGA infants in the discordant group was 34.4%, with no difference seen in the nondiscordant group (36%;  $p = .86$ ).

We assessed two other centile cut-offs (75th and 90th centiles). There were no differences in birthweight complications when these cut-offs were applied (data not shown).

**Table 1**

#### Baseline Characteristics

	Discordant ( $\geq$ 85th centile) <i>n</i> = 32	Not discordant (< 85th centile) <i>n</i> = 186	<i>p</i> value
Baseline details			
Mean maternal age — years ( $\pm$ std dev)	33.4 (3.6)	33.5 (3.9)	.93*
Treatment cycle — no. (25th–75th centile)	3 (1,6)	3 (1,5)	.99†
Embryos transferred — no. (range)	2 (2–4)	2 (1–4)	.19†
Gestational age at delivery in weeks (25th–75th centile)	36 (35,37)	36 (35,37)	.40†

Note: \* *t* test; †Mann-Whitney;

**Table 2**

#### Primary Birthweight Outcomes

	Discordant ( $\geq$ 85th centile) <i>n</i> = 32	Not discordant (< 85th centile) <i>n</i> = 186	<i>p</i> value
Outcomes			
Birthweight in grams — Mean ( $\pm$ SD)	2625 (392)	2442 (542)	.07*
SGA < 10th in at least one twin — no. (%)	11(34.4%)	67 (36.0%)	.86‡
Birthweight discordance > 20% — no. (%)	6 (18.8%)	33 (17.7%)	.89‡

Note: \* *t* test; ‡Chi-squared test

## Discussion

We found dichorionic twins discordant at 6–9 weeks of gestation, but liveborn over 24 weeks of gestation are not at increased risk of being either SGA, or discordant for birthweight.

While a number of studies have investigated the relationship between late first trimester CRL discordance and birthweight or other adverse outcomes, ours may be the first to focus on 6–9 weeks of gestation. Also, we may be the first to use true gestational age, rather than derived dates from ultrasound measurements and reference charts. To do this, we restricted our analysis to IVF conceptions.

We elected to calculate CRL discordance from absolute CRL lengths (Tai et al., 2007) rather than use differences in estimated gestational age calculated from published reference charts (Kalish et al., 2003). This was done in light of the fact we compared estimated dates derived from locally derived CRL reference charts (Australian Society of Ultrasound in Medicine) to true gestational age calculated from known conception dates in an IVF singleton cohort, and found significant differences (data submitted elsewhere).

Previous reports suggest CRL discordance at 10–14 weeks of gestation has a significant association with birthweight discordance of  $\geq 20\%$ . Kalish et al. (2003) investigated 130 twin pregnancies at 11–14 weeks of gestation. They used a 90th centile cut-off to define CRL discordance, which was equivalent to a CRL discordance of  $> 10\%$ . In the CRL discordant group, the incidence of birthweight discordance was 46%, compared to 9% among controls. Tai et al. (2007) investigated 178 twins at 7–14 weeks of gestation, an 85th centile cut-off was used to define CRL discordance, equivalent to a CRL discordance of  $> 11\%$ . Their results for dichorionic twins were remarkably similar to the findings reported by Kalish et al. (2003); a 41% incidence of birthweight discordance in the CRL discordant group, compared to 7.6% in the nondiscordant cohort. In addition, they found CRL discordance was associated with SGA, need for admission to neonatal intensive care unit and an increase in a composite of perinatal morbidity. However, not all reports have concluded that CRL discordance at 11–14 weeks is associated with birthweight discordance (Salomon et al., 2005).

In restricting our analysis to liveborn twins, we did not explore the relationship of CRL discordance at 6–9 weeks with the death of a single twin  $> 20$  weeks gestation. However, this is a rare outcome, complicating 0.5–6.8% of twin pregnancies (Burke et al., 1990) and is unlikely to have biased our primary findings.

Like Tai et al. (2007), we chose to focus on the growth of twins that reached viability and therefore excluded any losses under 24 weeks of gestation in our analysis. This means that a CRL discrepancy may still be associated with a risk of miscarriage. This premise is supported by studies of singletons where a shorter than expected CRL at 5–10 weeks of gestation

portends an increased risk of miscarriage (Mukri et al., 2008). However, our data does suggest should a pregnancy progress to viability despite early CRL discordance, there appears to be no significant risk of growth complications.

Our findings provide reassurance for clinicians that CRL discordance at 6–9 weeks of gestation is not associated with birthweight discordance, or SGA once the pregnancy reaches viability. However, the pregnancy may still be at immediate risk of miscarriage. In line with this and given previous reports, discussed above (Kalish et al., 2003; Tai et al. 2007), it may be prudent to repeat the ultrasound at 10–14 weeks of gestation.

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