Human Reproduction vol 7 no.8 pp.1170–1172, 1992

Incidence and significance of unequal gestational sac diameter or embryo crown–rump length in twin pregnancy

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The incidence of differences in gestational sac diameter and crown–rump length, measured at the time of the first ultrasound, in which at least one gestational sac or crown–rump length could be visualized, were analysed retrospectively in 260 twin pregnancies in which one or both fetuses were delivered at term. The difference in gestational sac diameter averaged 1.2 ± 0.1 mm for pregnancies which ended in twin births, compared to 2.0 ± 0.3 mm when pregnancy ended in single births ($P < 0.02$). The difference in crown–rump length averaged 2.4 ± 0.6 mm for pregnancies which ended in a single birth, compared to 0.9 ± 0.1 mm for twin births ($P = 0.02$). Disparities of ≥3 mm in gestational sac diameter ($P < 0.05$) or crown–rump length ($P < 0.001$) were associated with an embryo loss rate ≥50%. The disparity in gestational sac diameter ($P < 0.04$) and crown–rump length ($P < 0.01$) was smaller in pregnancies resulting from assisted reproductive technologies, compared with pregnancies resulting from coitus or insemination. Differences in gestational sac diameter and crown–rump length in early pregnancy were unrelated to differences in birth weight, length or sex.

Key words: crown–rump length/embryo/gestational sac/ultrasound/twin

Introduction

Ultrasound in early pregnancy reveals a higher incidence of multiple gestation in both spontaneous pregnancy and pregnancy after ovulation induction with clomiphene citrate or human menopausal gonadotrophin (HMG), than is indicated by births (Finberg and Birnholz, 1979; Schneider *et al.*, 1979; Dickey *et al.*, 1990; Kelly *et al.*, 1991). Resorption of one gestational sac occurs in 30–40% and of both sacs in 10–20% of spontaneous pregnancies (Finberg *et al.*, 1979; Dickey *et al.*, 1990), and in a lesser percentage of ovulation-induced pregnancies (Dickey *et al.*, 1990). We have observed that gestational sac diameter and crown–rump length are often unequal early in multiple gestations. In an effort to determine the extent and frequency of unequal gestational sac or embryo size and the relationship of these inequalities to pregnancy outcome, we retrospectively analysed the initial first trimester ultrasound findings in 235 twin gestations which resulted in the birth of at least one baby. The cases were part of an ongoing study of pregnancy outcome after infertility treatment begun in 1976 and which now comprises >5000 pregnancies.

Materials and methods

The computerized records of all patients who became pregnant as a result of infertility treatment at our clinic since 1976 were examined. The ultrasound findings during the first 8 weeks of 260 twin gestations, with an expected date of delivery before July 1, 1991, were analysed. Excluded from further analyses were 25 pregnancies (9.6%) which ended in spontaneous abortion of both gestational sacs or embryos. When feasible, all newly pregnant patients were scanned by ultrasound between 37 and 49 days of gestation and again 14 days later. From 1976 to 1987, trans-abdominal ultrasound was performed with a Technicare Auto Sector (Johnson and Johnson/GE, Milwaukee, WI, USA) using a 5.0 MHz transducer. After that date, vaginal ultrasound was performed using an ATL Ultramark 4 (Advanced Technology Laboratories, Inc., Bothell, WA, USA) and a 5.0 MHz intravaginal transducer. The gestational sac diameter (GSD) was measured in multiple planes and the average was recorded. All ultrasound scans were performed by one of the authors (E.M.M.). Crown–rump length (CRL) was measured, using the method described by Robinson (1973), once a heart rate could be determined. A GSD or a CRL ≥2 mm was measurable using vaginal ultrasound, compared with ≥5 mm using abdominal ultrasound. Cases were excluded from the analysis of GSD if the gestational age was >49 days and from analysis of CRL if gestational age was >63 days. At the beginning of the study period, a GSD was not recorded once a CRL was present. As a result, there were only 156 cases with a GSD available for analysis. In 65 cases, the initial ultrasound performed before a CRL was visible was not repeated, resulting in 180 cases available for CRL analysis.

Results are reported as differences in mm ± SEM between twins at the time of the first ultrasound examination at which a GSD or a CRL were detectable for either twin. Statistical analysis was by Fishers exact test, Pearsons correlation coefficient and Student's *t*-test. Results were considered significant at the 0.05 level.

Results

The average GSD for the larger twin was 8.0 ± 0.3 mm. The average difference in GSD between twins was 2.0 ± 0.3 mm for pregnancies which resulted in single births, compared to 1.2 ± 0.1 mm for twin births ($P < 0.02$). The relationship between differences in GSD in twin gestations and birth number is shown in Table I. No difference or ≤1 mm difference in GSD occurred in 52% of twin gestations. The difference in GSD was 1.5 to 2.5 mm in 14.7% of twin gestations and ≥3.0 mm in 14.1%. In 18% of patients, only a single sac was observed at the time of the first ultrasound. The percentage of twin gestations resulting in the birth of a single baby was increased when the difference in GSD was ≥3 mm (54.5%), compared with a difference ≤1 mm ($P < 0.05$). The percentage of single outcomes was not increased when a single sac was seen on the initial ultrasound. The average gestational age was identical, 39.6 days, at the time of the initial ultrasound, whether a single sac or two sacs were seen.

The average CRL for the larger twin was 8.4 ± 0.3 mm. The average difference in CRL between twins was 2.4 ± 0.6 mm for pregnancies which resulted in single births, compared to 0.9 ± 0.1 mm for twin births ($P = 0.02$). The relationship between differences in CRL of twin gestations and birth number is shown in Table II. No difference or ≤1 mm difference occurred in 50.5% of twin gestations. The difference in CRL was 1.5–2.5 mm in 11.7% of twin gestations and ≥3 mm in 7.8%. In 30% of patients, only a single CRL was observed initially. The percentage of single births was increased, compared to ≤1 mm difference, when the difference in CRL was ≥3 mm (50%) ($P < 0.001$) or when a single embryonic CRL was measurable on the first ultrasound (77.8%) ($P < 0.001$). The average gestational age was 50.0 ± 1.0 days when a single CRL was seen and 51.7 ± 0.5 days when two CRLs were seen at first ultrasound.

Smaller disparities in GSD and CRL were seen in pregnancies resulting from in-vitro fertilization (IVF) ($n = 14$) or gamete intra-Fallopian transfer (GIFT) ($n = 28$) than in pregnancies resulting from coitus or intrauterine insemination (IUI) after ovulation induction with clomiphene citrate ($n = 84$) or human menopausal gonadotrophin (HMG) ($n = 37$) (sac 1.0 ± 0.2 mm versus 1.6 ± 0.2 mm; $P = 0.05$) (CRL 0.7 ± 0.25 mm versus 1.3 ± 0.2 mm; $P < 0.01$). Differences in GSD and CRL at the time of the initial ultrasound were unrelated to differences in sex or in weight or length at birth in those pregnancies which resulted in twin deliveries.

Table I. Initial difference in diameter of twin gestational sacs ≤49 days from last menstrual period

Difference (mm)	Patients	%	Births			
			Twin no.	%	Single no.	%
None	27	17.3	19	70.4	8	29.6
≤1.0	55	35.2	38	69.1	17	30.9
1.5–2.5	23	14.7	13	56.5	10	43.5
≥3.0	22	14.1	10	45.5	12[a]	54.5
No second sac	29	18.6	21	72.4	8	27.6
Total	156	100.0	99	63.5	57	36.5

[a]Fishers exact test versus none or ≤1, $P < 0.05$.

Table II. Initial difference in twin crown–rump length ≤63 days from last menstrual period

Difference (mm)	Patients	%	Births			
			Twin no.	%	Single no	%
None	47	26.1	42	89 4	5	10.6
≤1.0	44	24.4	41	93.2	3	6.8
1.5–2.5	21	11.7	18	85.7	3	14.3
≥3.0	14	7.8	7	50.0	7**	50.0
No second embryo	54	30.0	12	22.2	42[a]	77.8
Total	180	100.0	120	66.7	60	33.3

[a]Fishers exact test versus none or ≤1 mm, $P < 0.001$.

Discussion

In the present study, differences of <3.0 mm between twins in GSD and CRL, at the time they could first be observed by ultrasound, were not associated with any significant increase in single births. Sixty-four per cent of twin gestational sac pregnancies ended in twin births in the present study. This is higher than the 37% twin births previously reported by Schneider *et al.* (1979) in a series of 78 twin pregnancies. We experienced no difficulty in distinguishing a second gestational sac from subchorionic fluid due to haemorrhage or other aetiologies. In a recent publication, we reported that subchorionic fluid could be found in 50% of single gestational sac pregnancies repeatedly scanned with vaginal ultrasound, during the first 12 weeks of gestation, and in 35% of pregnancies repeatedly scanned with abdominal ultrasound (Dickey *et al.*, 1992). Mistaken identification of subchorionic fluid as a gestational sac may explain the higher incidence of spontaneous reabsorption of the second gestational sac reported by Schneider *et al.* (1979) and others (Finberg and Birnholz, 1979; Kelly *et al.*, 1991).

We previously reported the outcome of 227 twin, 45 triplet and five quadruplet gestations diagnosed by first trimester ultrasound in a paper which included most of the patients in the present study (Dickey *et al.*, 1990). In that study, in contrast to Schneider *et al.* (1979), we found that resorption of one or both embryos occurred less often in twin pregnancies after ovulation induction with clomiphene citrate or HMG than after spontaneous ovulation (Dickey *et al.*, 1990). The probability of a singleton birth was 35% in pregnancies with clomiphene citrate ($n = 113$), compared to 60% for no medication ($n = 37$; $P < 0.02$), and 43% when treated with HMG ($n = 71$) for patients who did not have assisted reproduction (Dickey *et al.*, 1990). In the present study, we found no differences in average GSD or CRL in twins from clomiphene- or HMG-induced pregnancies, compared to spontaneous pregnancies. However, we noted smaller average differences in GSD and CRL of twins resulting from IVF and GIFT than in twins resulting from clomiphene citrate or HMG without assisted reproduction.

The differences between twins in GSD and CRL suggest that there may be a large degree of variability in the growth rate of

human embryos early in pregnancy. An alternative explanation for the differences in GSD and CRL between twins is that they are the products of ovulations separated in time by several days. Significant differences between twins in GSD and CRL, in the present study, were less when pregnancies resulted from IVF or GIFT, where eggs are retrieved and inseminated simultaneously, than when pregnancies resulted from spontaneous ovulation.

In triplet and quadruplet gestations, our findings are similar to those reported for twin gestations; however, the numbers of cases were too small to be statistically significant (unpublished). The findings of the present study and those of our previous study (Dickey *et al.*, 1990) may be of practical use to clinicians in counselling patients regarding the outcome of pregnancies when multiple gestational sacs or embryos are detected by first trimester ultrasound.

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Received on March 2, 1992; accepted on June 2, 1992