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First-trimester ultrasound examination and the outcome of monochorionic twin pregnancies

A. El Kateb, B. Nasr, M. Nassar, J. P. Bernard and Y. Ville*

Department of Obstetrics and Gynecology, Paris-Ouest medical school, UVSQ, CHI Poissy-Saint Germain en Laye, France

Objective To refine the incidence of abnormal first-trimester ultrasound measurements and their correlation with the outcome of monochorionic diamniotic pregnancies.

Methods First-trimester crown–rump length (CRL) and nuchal translucency thickness (NT) measurements were studied in three subgroups of a total of 200 monochorionic twin gestations referred to our center between June 2002 and February 2006. Intertwin CRL discordance was defined as >10% and the 95th percentile of NT thickness for gestational age was used.

The first group of 103 consecutive unselected monochorionic diamniotic twin pregnancies was prospectively followed up from 11–14 weeks onwards, throughout the pregnancy. The second group of 136 nonconsecutive monochorionic diamniotic twin pregnancies including 64 that developed TTTS was studied retrospectively. The third group of 100 consecutive cases of TTTS studied retrospectively for the correlation between first trimester measurements and staging and timing of occurrence of TTTS.

Results In group 1, the incidence of TTTS was 5 in 103 (5%, 95CI [0.7–9]). Large intertwin CRL discordance and increased NT were correlated with perinatal death. In group 2, no significant association was found between first-trimester parameters and the development of TTTS but discordance in early second trimester biometry and Doppler were. In group three, a positive correlation was found between the intertwin discordance in CRL and early occurrence of TTTS before 20 weeks of gestation ($p = 0.02$).

Conclusion Monochorionic twin gestations who ultimately develop TTTS may exhibit intertwin difference in growth as early as 11–14 weeks of gestation. The earlier the discordance the earlier the development of the disease.

KEY WORDS: monochorionic; first trimester; TTTS

INTRODUCTION

Fetal loss rate is much higher in monochorionic than in dichorionic pregnancies. The increased mortality in monochorionic pregnancies is likely to be at least in part a consequence of chorio-angiopagus and severe early onset of TTTS (Sebire *et al*., 2000). The relationship between first trimester ultrasound measurements especially early intertwin growth discordance and the outcome of these pregnancies is controversial and is derived from relatively small series (Sebire *et al*., 1997a, 1998, 2000; Kalish, 2003; Deter *et al*., 1999; Salomon *et al*., 2005).

TTTS occurs in approximately 5.5% to 17.5% of all monochorionic pregnancies and is defined sonographically by the combination of polyhydramnios in one sac and oligohydramnios in the other sac in monochorionic diamniotic twin gestations (Quintero, 2003). Intertwin anastomoses on the chorionic plate are responsible for the development of a net imbalance in blood flow between two monochorionic fetuses and subsequent development of TTTS (Sebire *et al*., 1998).

The aim of this study was to refine the incidence of abnormal first-trimester ultrasound measurements and their correlation with the outcome of monochorionic diamniotic pregnancies.

METHODS

Our institution is a referral center for multiple pregnancies and especially so for monochorionic twins complicated by twin-to-twin transfusion syndrome. We have therefore classified cases according to the prospective or largely retrospective nature of the analysis of pregnancies and perinatal outcomes once referred to our unit.

These three groups are necessary in order to limit biases introduced by the indication for referral. Each case reported is counted only once and in only one of the three groups.

Twin-to-twin transfusion syndrome was defined by the association of polyuric polyhydramnios in one sac with a deepest vertical pool of amniotic fluid (dvpaf) of at least 8 or 10 cms before and after 20 weeks respectively together with oligo-uric oligo-hydramnios in the other sac with a dvpaf of at most 2 cm. Staging of the disease was done at presentation accordingly with Quintero's classification (Quintero, 2003).

Crown-rump length (CRL) and nuchal translucency thickness (NT) were measured to the nearest millimeter in a sagittal section of the fetus with the head in a neutral position (Sebire *et al*., 1997a; Whitlow *et al*., 1998).

*Correspondence to: Y. Ville, Department of Obstetrics and Gynecology, Paris-Ouest medical school, UVSQ, CHI Poissy-Saint Germain en Laye, France. E-mail: yville@wanadoo.fr

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Intertwin discordance in the first trimester of pregnancy was defined as a difference >10% between CRLs (Salomon *et al*., 2005)

Intrauterine growth restriction was defined by birthweight <5th percentile. Growth discordance at birth was defined by a difference in birthweight >20%.

Two hundred monochorionic diamniotic twin pregnancies were seen at our center between June 2002 and February 2006, in which both CRL and NT measurements were recorded at 11–14 weeks of gestation were studied using three different approaches. Cases with chromosomal abnormalities or congenital malformations were not included.

A first group of 103 consecutive unselected monochorionic diamniotic twin pregnancies was prospectively studied and followed-up within our perinatal network throughout the pregnancy from 11–14 weeks of gestation onwards and at 2-week intervals up until delivery. Intertwin discordance in CRL and NT measurements were evaluated for possible relation with the outcome of pregnancy including the development of TTTS, intrauterine growth restriction (IUGR) and perinatal mortality which was calculated as the number of intrauterine deaths, intrapartum deaths and neonatal deaths before seven days per thousand children born with a gestational age of 22 or 24 weeks or more.

A second group comprised of 136 nonconsecutive monochorionic diamniotic pregnancies that were referred to our unit in the second or third trimester and were studied retrospectively when both first and early second trimester ultrasound measurements at between 11–14 and at 16–18 weeks respectively were available. This included 64 cases that developed TTTS and 72 that did not and were used as a control population.

CRL intertwin discordance and NT measurements were evaluated for a possible relation with the development of TTTS. Intertwin discordance in abdominal circumference (AC) and Umbilical Doppler PI measurements in the second trimester were also studied to evaluate differences between cases that developed TTTS and controls.

A third approach consisted of the retrospective analysis of 100 cases of TTTS for intertwin discordance in CRL and NT measurements at 11–14 weeks and their relation with subsequent staging and timing of occurrence of TTTS. These were referred to our institution for fetal therapy when TTTS was diagnosed.

RESULTS

TTTS developed in 5 of the 103 unselected monochorionic diamniotic twin pregnancies (Group 1) that underwent serial ultrasound examination every fortnight from 11–14 weeks up until delivery (5%, 95%CI[0.7–9]).

In all 206 fetuses studied (103 twin pregnancies), intertwin discordance of at least 10% in CRL and above the 95th percentile NT thickness for gestational age was found in 14 (7%), 95% CI (2.07–11.93) and 10 (5%), 95% CI (0.79–9.21) of the all fetuses respectively (Figures 1 and 2).

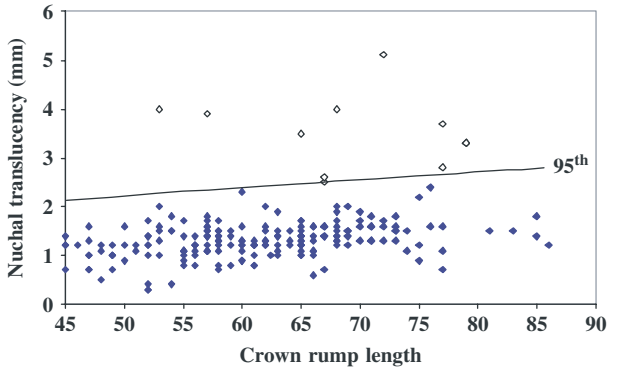

Figure 1—Scatter diagram of nuchal translucency and crown rump length for the studied fetuses showing the relation to the 95th percentile reference value in 103 consecutive unselected monochorionic diamniotic twin pregnancies was prospectively followed up from 11–14 weeks onwards, throughout the pregnancy (group 1)

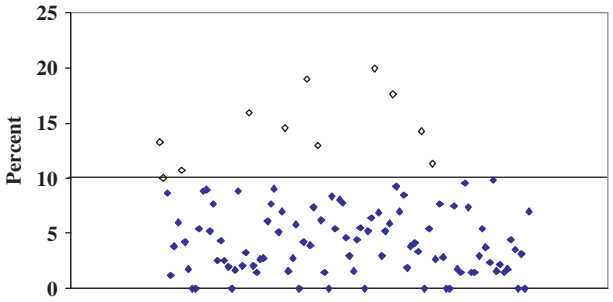

Figure 2—Dot plot for the CRL discordance as a percent of the larger twin in 103 consecutive unselected monochorionic diamniotic twin pregnancies was prospectively followed up from 11–14 weeks onwards, throughout the pregnancy (Group1)

In this prospective study, there was no significant relationship between discordance in CRL and the development of TTTS [8 (4%) vs 2 (14%)] or IUGR [25 (13%) and 2 (14%)]. TTTS developed in 8 (4%) and in 2 (20%) fetuses with NT thickness <95th and >95th percentile for gestation respectively (NS). Similarly there was no correlation between NT thickness at 11–14 weeks' and the development of IUGR [25 (13%) vs 2 (20%)].

However, perinatal deaths were more common in cases with early discordance in CRL >10% and in those with at least one twin showing NT thickness >95th percentile [9 (5%) vs 7 (50%) fetuses] ($p = <0.001$) and [13 (7%) vs 3 (30%) fetuses] ($p = 0.049$) respectively.

Among 136 monochorionic diamniotic twin pregnancies studied retrospectively (Group 2), including 64 that developed TTTS and 72 that did not, intertwin discordance in CRL >10% and NT thickness >95th percentile were not correlated with the development of TTTS or IUGR.

However discordance >20% in abdominal circumference and a high Umbilical Doppler PI >1.8 at 18 weeks were found more frequently in pregnancies that eventually developed TTTS [25 (40%) vs 5 (7%)] ($p = <0.001$[chi2/Fischer] and [32 (50%) vs 16 (22%)] ($p = 0.001$ [chi2/Fischer]) respectively.

In 100 cases of TTTS referred for laser treatment from 33 different institutions and analyzed retrospectively

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(Group 3), the syndrome developed before 20 weeks of gestation in 60 cases (60%). Intertwin discordance in CRL >10% at 11–14 weeks was found more often in cases occurring earlier [14 (88%) vs 2 (12%)] ($p = 0.02$). The presence of NT thickness >95th percentile was not correlated with gestational age at diagnosis of TTTS and staging at diagnosis showed no correlation with first trimester ultrasound findings.

DISCUSSION

All monochorionic twin pregnancies are characterized by the presence of vascular anastomoses between the two fetoplacental circulations, but circulatory imbalance resulting in TTTS has been described in about 15% of these cases and this complication may manifest with first- and second-trimester ultrasound markers (Sebire *et al*., 1997a). First trimester fetal growth is thought to occur at a constant exponential rate with little biological variation (Deter *et al*., 1999). However unequal distribution of fetoplacental perfusion in monochorionic twin gestations may significantly affect growth and hemodynamics early in gestation.

Although studies on this topic are scarce and most statistics were drawn mainly from one cohort (Sebire *et al*., 1998, 2000), our results may lead to somehow different conclusions. The incidence of TTTS in otherwise unselected monochorionic twin pregnancies was 5%, when Sebire's prospective study suggested a higher incidence among 132 cases (12%, 95% CI [6.55–17.69]). Owing to the small size of both series (103 vs 132), comparison of confidence intervals shows that quite large variations in this incidence can be expected (NS $p = 0.088$). In Sebire's series, intertwin disparity in size was not a risk-factor for developing TTTS but NT thickness above the 95th percentile in at least one twin was (Sebire *et al*., 1998, 2000). We found that cases with intertwin disparity in size are at increased risk of developing TTTS and that the earlier the discordance, the earlier the development of TTTS. Although the methodology used in Sebire's paper, a prospective longitudinal follow-up, makes its conclusions stronger, some associations with adverse outcome of rare occurrence (5–15%) such as twin-to-twin transfusion syndrome may only become apparent in either much larger cohorts of monochorionic pregnancies, not reported to date, or may require to examine, even retrospectively, large populations of abnormal cases together with a control population. This justifies the approach we have used to study independently three relatively large groups of monochorionic twin pregnancies including one prospectively and two retrospectively. They allowed for different aspects to be examined using different methodologies. Furthermore, the predictive value of increased NT thickness >95th percentile, although appealing to the suspected pathophysiology of the disease, might have been overemphasized by reporting the experience of a referral center for cases with increased NT. This is also suggested by the lower incidence of increased NT thickness >95th percentile in our population although this is also not different from Sebire's results when accounting for confidence intervals and sample sizes.

In a previous study on normal twin pregnancies, excluding cases that subsequently developed TTTS, discordance in CRL of less than the 95th percentile was not associated with adverse perinatal outcome but twins with a larger discordance had a poor outcome (Salomon *et al*., 2005). Considering that perinatal mortality in twins is 2–4-fold that in singletons (Westergaard *et al*., 2000) and that fetal loss rate in monochorionic twins is up to five-fold higher than in dichorionic pregnancies (Sebire *et al*., 2000; Sperling *et al*., 2006), early discordance of CRL >10% should probably heighten fetal surveillance in a dedicated twin pregnancy clinic.

However, we acknowledge that the population of monochorionics we have gathered in this study may also be biased towards a higher incidence of perinatal mortality and morbidity especially in cases analyzed retrospectively for first-trimester characteristics although our data are within expected figures. It has been shown that fetal outcome is worse for monochorionic than dichorionic twins which has been attributed mainly to complications that are caused by placental vascular anastomoses (Sebire *et al*., 1997b; Snijder and Wladimiroff, 1998). In a study that involved 300 pregnancies, the perinatal mortality rate was found to be 16% in the monochorionic group compared with 11% and 1% in the dizygotic and monozygotic dichorionic groups respectively; 88% of the deaths in the monochorionic group were related to twin–twin transfusion (Machin *et al*., 1995). In another study that involved 1008 twin pregnancies, the perinatal mortality rate was 6.5% in the monochorionic group compared with rates of 2.2% and 2.6% in the dizygotic and monozygotic dichorionic pregnancies, respectively (Dube *et al*., 2002). In this same study, the incidence of birth weight discordancy was 8.6% in the monochorionic group and 7.3% and 5.4% in the dizygotic and monozygotic dichorionic groups respectively. Sebire *et al*. compared perinatal loss rate in monochorionic and dichorionic pregnancies, they found that the risk of loss my be increased six-fold in the monochorionic group (12.2% for monochorionic twins vs 1.8% for dichorionic twins) (Sebire *et al*., 1997b). Adegbite *et al*. compared monochorionic and dichorionic twins born between 24 and 34 weeks gestation and found that MC placentation was associated with significant increases in the incidence of cerebral palsy (8% vs 1%) and neurologic morbidity (15% vs 3%). Impaired neurodevelopment in the monochorionic twins was significantly increased when associated with discordant growth (42%), twin-twin transfusion syndrome (37%), or co-twin death (60%) in a comparison with MC twins with concordant growth (8%) (Adegbite *et al*., 2004).

Because monochorionic pregnancies are less than 0.5% of all pregnancies, a large prospective ultrasound-based follow-up study is unlikely to be available in the near future. Therefore these results and those already published call for systematic reviews of small prospective series as well as registries of monochorionic pregnancies established prenatally from as early as the first trimester of pregnancy.

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