



Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive



INSTITUTE OF OBSTETRICIANS
& GYNAECOLOGISTS
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

CLINICAL PRACTICE GUIDELINE

MANAGEMENT OF MULTIPLE PREGNANCY

Institute of Obstetricians and Gynaecologists,
Royal College of Physicians of Ireland
and
Directorate of Strategy and Clinical Care,
Health Service Executive

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Key Recommendations

1. Where multiple gestation is identified on ultrasound examination, chorionicity should be assigned at the earliest opportunity. This is best achieved before 14 weeks gestation.
2. A record should be retained of the ultrasound image that supports assignment of chorionicity and a second opinion should be sought if there is uncertainty.
3. If chorionicity cannot be determined, monochorionicity should be assumed until proven otherwise, and a strategy of prenatal surveillance that includes screening for twin-twin transfusion syndrome should be adopted accordingly.
4. Prenatal and perinatal care should be hospital-based for all multiple gestations, coordinated by an obstetrician experienced in the management of multiple gestation.
 - 4.1. Indications for referral to a tertiary level Fetal Medicine Unit:
 - 4.2. Suspected monoamnionicity
 - 4.3. Suspected twin-twin transfusion syndrome
 - 4.4. Fetal structural abnormality
 - 4.5. Suspected intertwin growth-discordance >18%
 - 4.6. Higher-order multiple gestation
 - 4.7. Single fetal demise in a monochorionic twin gestation
5. Monochorionic twin gestation should be regarded as 'high-risk' and merits ultrasound examination every 2 - 3 weeks from 16 weeks gestation as a means of screening for twin-twin transfusion syndrome and fetal growth restriction.
6. Pregnancies complicated by twin-twin transfusion syndrome prior to 26 weeks gestation should be considered for laser ablation of communicating placental vessels as such therapy yields better perinatal outcomes than management by serial amnioreduction.
7. In the case of uncomplicated dichorionic twin gestation, serial growth evaluation should be performed at least every 4 weeks from 24 weeks gestation.
8. Although mid-trimester determination of cervical length may predict preterm birth in twins, such evaluation is not recommended, on the basis that there is no preventative intervention that has been shown to reduce the risk of spontaneous preterm twin birth. Specifically, there is no evidence to support bed rest, elective placement of cervical cerclage, ultrasound-indicated cerclage, prophylactic tocolytic therapy or progesterone for the purpose of prevention of preterm twin birth.
9. A course of antenatal corticosteroid therapy should be prescribed in the event of anticipated preterm delivery prior to 34 weeks gestation, accepting that the benefit of antenatal corticosteroids in the prevention of respiratory morbidity may be less than that observed in singleton pregnancies. Corticosteroid therapy

should be administered in a 'timed' rather than in an untargeted ('routine') manner.

10. Applying a strategy of close fetal surveillance, perinatal morbidity can be minimised by allowing uncomplicated monochorionic twin pregnancies continue to 37 weeks' gestation and dichorionic twins to 38 weeks. Among monochorionic twins, it must be acknowledged that this approach is balanced against a 1.5% risk of late in-utero death.
11. Mode of twin delivery should be considered on the basis of individual case characteristics to include comorbidity, gestational age, availability of expertise in the management of vaginal twin birth, and patient preference.
12. Where no contraindications exist, monochorionic or dichorionic twins may be considered for vaginal birth. Women should be informed that where the first twin delivers by the vaginal route, the prospect of requiring a caesarean section for delivery of the second twin is approximately 4%.
13. An obstetrician experienced in vaginal twin birth should be immediately available in the event of twin labour.

1. Purpose and Scope

The purpose of this guideline is to improve and standardize the management of multiple pregnancy in obstetric units in Ireland.

These guidelines are intended for healthcare professionals, particularly those in training, who are working in HSE-funded obstetric and gynaecological services. They are designed to guide clinical judgement but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the woman.

2. Background and Introduction

Multiple gestation is increasingly common, owing in part to advances in reproductive technology. Twin births currently represent approximately 1.8% of all births in Ireland, an increase from 0.8% in 1989 (Smith et al, 2010). Multiple pregnancy is known to confer increased perinatal risk, including mortality, preterm birth, congenital abnormalities, fetal growth restriction and twin-twin transfusion syndrome. Twins are four times more likely than singletons to develop cerebral palsy (Donovan et al, 1998).

Intrauterine growth restriction affects at least one twin in 14 – 25% of twin pregnancies (Jewell and Yip, 1995). Furthermore, many maternal obstetric morbidities, such as haemorrhage, proteinuric hypertension and gestational diabetes, are observed more commonly in the setting of multiple gestation. Optimal perinatal management is aimed at reducing such morbidity. To this end, prenatal and perinatal care of multiple pregnancy should comprise a hospital-based model, to include frequent maternal and fetal surveillance and formulation of an individualised delivery plan.

3. Methodology

Medline, EMBASE and Cochrane Database of Systematic Reviews were searched using terms relating to multiple gestation, twin pregnancy, prenatal care, labour and delivery complications, higher order multiple gestation. Searches were limited to humans and restricted to the titles of English language articles published between 1982 and 2012.

Relevant meta-analyses, systematic reviews, intervention and observational studies were reviewed. Particularly pertinent in the Irish setting are the data gleaned from the large prospective ESPriT Study (Evaluation of Sonographic Predictors of Restricted growth In Twins) conducted between 2007 and 2009, which offers contemporaneous twin data from eight tertiary referral obstetric units in Ireland.

Guidelines reviewed included NICE guideline on Multiple Pregnancy (September 2011), Royal College of Obstetricians and Gynaecologists guideline on Management of Monochorionic Twin Pregnancy (Guideline No 51; December 2008), American College of Obstetricians and Gynecologists Practice Bulletin No 56: Multiple Gestation: Complicated Twin, Triplet, and High-Order Multifetal Pregnancy (October

2004) and Royal Australian and New Zealand College of Obstetricians and Gynaecologists guideline on Management of Monochorionic Twin Pregnancy (C-Obs 42; March 2011).

The principal guideline developer was Dr Fionnuala Breathnach, Consultant Obstetrician/ Gynaecologist at the Rotunda Hospital and Senior Lecturer in Maternal Fetal Medicine, Royal College of Surgeons in Ireland. The guideline was peer-reviewed by Dr Liz Dunn (Wexford), Professor Sean Daly (Coombe), Dr Michael Gannon (Mullingar), the Institute's Clinical Advisory Group.

4. Clinical Guidelines

4.1 Diagnosis of multiple pregnancy

Perinatal outcome in multiple pregnancy is largely driven by chorionicity, the accurate assignment of which is therefore of critical importance. Where multiple pregnancy is identified on ultrasound examination, the chorionicity and amnionicity of the pregnancy should be determined at the earliest opportunity. **This is best achieved before 14 weeks gestational age**, by determining the number of placental masses, the lambda or T-sign and thickness of the intertwin membrane. **If in doubt, a second opinion should be sought.**

This differentiation becomes more difficult later in gestation and, in the setting of concordant fetal gender, it may not be possible to confidently assign chorionicity. Under such circumstances, the pregnancy should be described as of 'undetermined chorionicity' and monochorionicity should be assumed until proven otherwise. **When chorionicity is assigned, a photographic record of the ultrasound image that supports that assignment should be kept in the woman's record.**

4.2 Delivery of Antenatal and Perinatal Care

Antenatal and perinatal care of multiple pregnancies should be hospital-based, delivered by a team that includes obstetricians, ultrasonographers, neonatologists and midwives, all experienced in the management of multiple gestation. A clear pathway should be in place for referral in the case of suspected complications (see 5.4).

4.3 Preterm Delivery

The median gestational age for delivery of twins in Ireland is 37.1 weeks, with 20% of monochorionic twins and 7% of dichorionic twins delivering prior to 32 weeks' gestation. The ESPRiT Study (Evaluation of Sonographic Predictors of Restricted growth In Utero), a prospective multicenter observational study of twin pregnancy in Ireland, reported that in the interval between 24 and 28 weeks gestation, 5% of monochorionic and 1.5% of dichorionic twins were delivered (Breathnach et al, 2012).

Identification of a shortened cervical length may be predictive of spontaneous preterm labour in twins; Guzman et al (2000) have shown that 50% of twin gestations with a cervical length <20mm identified at 15-24 weeks gestation delivered before 32 weeks. A further study showed that a cervical length of <25mm at 24 weeks was associated with an increased risk of preterm birth before 32, 35 and 37 weeks' gestation (Goldenberg et al, 1996). **However, until such time as an intervention is identified that reduces the risk of preterm birth in twins, cervical length measurements are rendered unhelpful and not recommended.**

Specifically, the following interventions aimed at reducing the risk of preterm birth in multiple pregnancy have been studied and are considered not to reduce the risk of preterm labour in twins: bed rest (Crowther, 2010), prophylactic cervical cerclage (Dor et al, 1982), ultrasound-indicated cervical cerclage (Berghella et al, 2005), vaginal progesterone therapy (Norman et al, 2009), intramuscular progesterone (Combs et al, 2011; Durnwald et al, 2010) and tocolytic therapy (Yamasmit et al, 2005).

A course of antenatal corticosteroids may reduce the risk of respiratory morbidity, necrotising enterocolitis and intraventricular haemorrhage in multiple pregnancy, but such preventative therapy should be timed and not given in an untargeted ('routine') manner. Furthermore, it should be acknowledged that the efficacy data for antenatal corticosteroids in multiple gestations are not as robust as those reported for singleton populations (Roberts et al, 2006).

4.4 Indications for referral to a tertiary-level Fetal Medicine Unit

At the discretion of a consultant obstetrician the following criteria should be considered to merit referral to a tertiary level Fetal Medicine Unit, for which a clear pathway should be in place in every obstetric unit that manages multiple gestation:

Suspected monoamnionicity

If monoamnionicity is confirmed, the pregnancy should be managed by the Fetal Medicine team.

Suspected feto-fetal transfusion syndrome

In the case of suspected feto-fetal transfusion syndrome, referral to a Fetal Medicine Unit should be made on an urgent basis.

Fetal structural abnormality

Fetal structural abnormality occurs more commonly among monochorionic twin gestations than among singleton pregnancies. This scenario can present a challenging management dilemma, in particular when the abnormality is associated with polyhydramnios, thus carrying the potential for preterm delivery. In addition, in-utero demise may occur, with consequent risk of severe hypotension and its attendant sequelae for the normal co-twin. Evaluation of such risks merits referral to a Fetal Medicine Centre.

Suspected intertwin growth-discordance >18%

Placental pathology commonly accounts for growth-discrepancy within a multiple pregnancy. Discordant fetal growth is usually defined as a 15-25% reduction in the estimated fetal weight of the smallest fetus compared to the largest (Talbot et al, 1997). Most published studies focus on discordant growth within twin pairs and have demonstrated an association with structural malformations, perinatal mortality, fetal growth restriction, preterm delivery, caesarean delivery for nonreassuring fetal status, umbilical arterial acidemia, NICU admission and respiratory morbidity (Breathnach et al, 2011, Roberts et al, 2006, Powers et al, 1994, Donovan et al, 1998). The prospective ESPRiT Study conducted in Ireland established that the threshold for significant birth weight discordance, i.e. that associated with an increase in perinatal morbidity, is 18% both for dichorionic twins and for monochorionic twins without twin-twin transfusion syndrome (Breathnach et al 2011). An anticipated difference of 18% or more between co-twin weights should therefore prompt more intensive fetal monitoring and merits consultation with a Fetal Medicine Specialist particularly before term.

Higher-order multiple gestation

Where more than two fetuses are identified on ultrasound examination, the woman should be referred to a Fetal Medicine Centre. Referral at the earliest opportunity will facilitate accurate assignment of chorionicity.

Single fetal demise in a monochorionic twin gestation

In the event of in-utero demise of one twin in a monochorionic twin gestation, neurological injury may occur in the surviving twin. This has been reported to occur as early as 12 weeks gestation (Weiss et al, 2004). Adverse neurological outcomes, such as multicystic encephalomalacia, are reported to occur in approximately 18% of surviving twins after the death of a co-twin (Ong et al, 2006).

In addition, in-utero fetal demise in one twin of a monochorionic pair confers a risk of co-twin demise that is approximately 12% (Ong et al, 2006), such that the cumulative risk of either co-twin death or severe neurological injury in a surviving co-twin is 30%. Such sequelae exist as a consequence of shared placental vasculature in a monochorionic gestation and are thought to result from severe hypotension in the co-twin which occurs at the time of demise of one twin.

In the event of suspected imminent single twin demise in a monochorionic gestation, such risks must be balanced against the risks of prematurity associated with iatrogenic delivery. At a very preterm gestation, the decision to manage such a pregnancy expectantly or to consider preterm delivery can be challenging, and merits input from a specialist Fetal Medicine service.

4.5 Ultrasound surveillance

For uncomplicated monochorionic twin pregnancy, the frequency of antenatal hospital visits should be every 2-3 weeks from 16 weeks' gestation until delivery (RCOG 2008, ACOG 2004, RANZCOG 2011) to include an ultrasound examination that includes formal fetal weight estimation and screening for ultrasound stigmata of twin-twin transfusion syndrome at each visit.

In the case of uncomplicated dichorionic twin gestation, prenatal consultations should coincide with ultrasound examinations with scheduled visits at least every 4 weeks from 24 weeks' gestation until 36 weeks' gestation and weekly thereafter (NICE 2011).

Twins with identified fetal growth restriction, reduced amniotic fluid volume in one or more amniotic sacs, or maternal complications such as preeclampsia should undergo more intensive fetal surveillance.

4.6 Twin-twin transfusion syndrome

Where possible, twin-twin transfusion syndrome presenting before 26 weeks gestation should be treated by selective laser photocoagulation of placental anastomoses rather than by amnioreduction. The randomised Eurofetus trial (Senat et al, 2006) reported fewer perinatal deaths and more babies alive at 6 months without neurologic morbidity in the laser group compared to those managed with serial amnioreduction.

4.7 Timing of Delivery

Several retrospective studies examining the risk and consequences of single twin death in a monochorionic pair and have led to an argument for apparently uncomplicated monochorionic twin pairs to be electively delivered once the sequelae of preterm delivery are perceived to be low, such as delivery at 32 (Barigye et al, 2005), 34 (Lee et al, 2008) or 36 weeks of gestation (Simoes et al, 2006, Hack et al, 2008). Other factors may have to be taken into account, for example, previous laser ablation or access to a Neonatal Intensive Care cot. Elective preterm delivery of uncomplicated monochorionic twins is aimed at minimising the risk of unanticipated in utero fetal demise at a later gestational age. However, the above-listed retrospective series have not examined the neonatal consequences of this strategy.

The large prospective ESPRiT study sought to identify the optimum gestational age for elective delivery of uncomplicated monochorionic and dichorionic twin pregnancies by determining the neonatal risk associated with elective delivery at each gestational age in the late third trimester and to ascertain the prospective risk of death or severe perinatal morbidity in ongoing pregnancies (Breathnach et al, 2012).

ESPRiT quantified the risk of subsequent in-utero fetal demise among monochorionic twin pregnancies at 1.5% at 34 weeks or 1.7% at 35 weeks' gestation. While elective delivery at 34 or 35 weeks' gestation abolishes that specific risk, that decision incurs a cost of neonatal morbidity that translates into an 88% NICU admission rate at 34 weeks, falling to 9% at 38 weeks. Neonatal morbidity among such elective preterm deliveries was predominantly respiratory and transient, but the potential for such morbidity should be discussed with parents when the timing of elective twin delivery is being considered.

In the case of dichorionic twins, the risk of in-utero fetal death in the third trimester is much lower (there were no deaths among dichorionic twins after 33 weeks in the ESPRiT cohort). Furthermore, the absence of interdependence of placental vasculature confers a lesser threat to the pregnancy in its entirety. A composite

measure of perinatal morbidity in the ESPriT dichorionic cohort fell from 7% at 36 weeks to 1% at 38 weeks gestation. The decision, therefore, to proceed with elective preterm delivery of an appropriately grown concordant dichorionic twin pregnancy before 38 weeks should be taken only after consideration of these neonatal morbidity risks.

Applying a strategy of close fetal surveillance, perinatal morbidity can be minimised by allowing uncomplicated monochorionic twin pregnancies continue to 37 weeks' gestation and dichorionic twins to 38 weeks. Among monochorionic twins, it must be acknowledged that this approach is balanced against a 1.5% risk of late in-utero death. If elective preterm delivery is offered prior to these suggested gestational ages, a timed course of antenatal corticosteroids should be administered.

4.8 Mode of Delivery

Neonatal outcomes following vaginal birth of twins versus caesarean delivery have been the subject of several retrospective series (Gocke et al 1989, Adam 1991, Grisaru 2000, Schmitz 2008, Fox 2010) and meta-analyses (Hogle 2003, Crowther 2000) as well as one small randomised trial (Rabinovici 1987). These studies have not provided evidence to support caesarean in favour of vaginal delivery, yet large population-based studies (Smith 2002; Wen 2004; Yang 2005; Smith 2005; Smith 2007; Armson 2006) have demonstrated an increased risk for neonatal morbidity and mortality of the second twin undergoing vaginal delivery.

In an Irish setting, prospective ascertainment of neonatal outcome data for the ESPriT study did not demonstrate an increase in delivery-related morbidity or mortality among twins exposed to a trial of labour (Breathnach et al 2011). This experience may be a consequence of very low overall levels of mortality or serious morbidity in this cohort of 1728 infants. Where trial of labour was considered, the successful vaginal delivery rate was 77%. **When the presenting twin delivered by the vaginal route, the prospect of requiring a caesarean delivery for the non-presenting twin was 4%.**

Mode of twin delivery should therefore be considered on the basis of individual case characteristics to include comorbidity, gestational age, availability of expertise in the management of vaginal twin birth, and the woman's preference.

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6. Implementation Strategy

- Distribution of guideline to all members of the Institute and to all maternity units.
- Implementation through HSE Obstetrics and Gynaecology programme local implementation boards.
- Distribution to other interested parties and professional bodies.

7. Key Performance Indicators

- Accuracy of assignment of chorionicity ascertained through correlation with placental pathology findings.
- Number of cases of twin-twin transfusion syndrome and perinatal outcome, including timing of diagnosis and therapy.
- Gestational age at delivery of monochorionic and dichorionic twins.
- Vaginal delivery rate among twin pregnancies undergoing trial of labour.
- Combined vaginal-caesarean delivery rate (i.e. caesarean delivery for 'second twin').
- Incidence of fetal growth restriction and growth discordance at birth, both anticipated and unanticipated.

8. Qualifying Statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advising women of their choices and ensure informed consent is obtained.
- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.