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Guidelines On Management of Multiple Pregnancies: Part II

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1 AIM

Part II of the guideline aims to examine the specific antenatal complications related to particular types of twin pregnancies, the timing and the mode of delivery, the intrapartum management of vaginal deliveries of twins, and the controversy of delayed interval delivery of the second twin in very preterm gestation.

2 SPECIFIC ANTENATAL COMPLICATIONS RELATED TO THE TYPE TO TWINS

a. Dichorionic (DC) twins:

i. Discordant fetal growth

The indication for delivery should take into consideration of the fetal well-being(s), the gestational age and serial growth velocity in case of discordant fetal growth.

In multiple pregnancies, discordance in fetal growth is calculated by dividing the difference in the estimated weights of the fetuses by the weight of the larger fetus [1]. In DC pregnancies, some form of difference in the fetal size can be normal as both fetuses may have different genetic make-up, especially if both still have normal parameters for the gestational age. It has been shown that the risk of fetal death begins to increase progressively when the weight discordance exceeds 25% [2]. Hence, it appears logical to offer close fetal surveillance if the discordance exceeds 20-25% [1]. Discordant fetal growth can be due to different genetic growth potentials, structural anomaly of one fetus, or an unfavourable placental implantation. The indication for delivery should take into consideration of the fetal well-being(s), the gestational age and serial growth velocity rather than the percentage of the discordance.

ii. Single intrauterine fetal demise (IUFD)

The cause of intrauterine death and the gestational age are the two main determining factors in the clinical decision of delivery or expectant management.

The decision to deliver the pregnancy or to adopt expectant management in case of single IUFD in DC pregnancies depends on the cause of the intrauterine fetal death and the gestational age. As the placentas are separate, there is no worry of damage to the surviving twin due to hypotensive or embolic phenomena, as in the case of monochorionic (MC) pregnancies. If the cause of the intrauterine fetal death is unlikely to result in problem of the surviving twin or the gestational age is remote from term, expectant management is appropriate and the neonatal outcome is usually good [3]. Although maternal disseminated intravascular coagulopathy after IUFD is a potential risk, it is extremely rare [4].

b. Monochorionic diamniotic (MCDA) twins:

i. Twin-twin transfusion syndrome

Monochorionic pregnancies should be monitored closely with ultrasonography for development of TTTS.

Twin-twin transfusion syndrome (TTTS) is a severe condition that complicates up to 15% of all MCDA pregnancies [5]. It is believed to occur as the result of uncompensated arteriovenous anastomoses in the placenta, leading to a net flow of blood from one twin to the other [6]. The

donor twin is usually anaemic, growth restricted and oliguric with oligohydramnios; whereas the recipient twin is usually plethoric, polyuric with polyhydramnios and may develop congestive heart failure and fetal hydrops. It can occur at any time during pregnancy but severe cases which present before 26 weeks are associated with high risks of perinatal mortality and handicap among the survivors [7-9]. Untreated, the perinatal mortality is up to 90% [5].

Prenatal diagnosis of TTTS is based on sonographic features of inter-twin blood flow discordance, including polyhydramnios (≥8cm vertical pocket) and a full bladder due to polyuria in the recipient, and severe oligo- or anhydramnios (≤1 or 2cm vertical pocket) in the donor with small or absent bladder filling [10, 11]. Discordant fetal growth is commonly seen in TTTS but is not an essential diagnostic feature. As it only occurs in MC pregnancies, the diagnosis of chorionicity in early pregnancy is important. Great discrepancy in the nuchal translucency thickness [8], inter-twin membrane folding [12] and disparity in fetal size in MC pregnancy [13] might be early signs of TTTS in the first trimester. Even if the first trimester scan is normal, regular ultrasonography at ~2 weeks' interval between 16 and 26 weeks is advised [10]. If TTTS is suspected, patient should be referred to a specialized fetal medicine centre for prompt assessment.

The main treatment options for TTTS include fetoscopic laser coagulation of the communicating placental vessels and serial amniodrainage. Fetoscopic laser therapy is technically more demanding and should be performed in specialized fetal medicine centres [14]. It has been shown in a randomized trial to offer higher survival rate and better neurological outcome among survivors during the first 6 months of life for TTTS diagnosed before 26 weeks of gestation, compared with amniodrainage [11]. Serial amniodrainage, on the other hand, is technically simpler. It should be offered in situations when laser therapy is technically difficult or not available, or when TTTS is diagnosed after 26 weeks [5].

ii. Single intrauterine fetal demise

Single IUFD in MC pregnancies carries significant risks to the surviving co-twin.

In MC pregnancies, single IUFD poses a significant risk to the surviving co-twin, mainly due to acute hypotensive episode at the time of the fetal demise [15]. The risks of perinatal mortality and serious neurological impairment among survivors have been reported in 30% and 10-20% of cases respectively [3, 16]. If single IUFD occurs after successful fetoscopic laser therapy for TTTS, the risk of damage to the surviving twin is lower [17]. The best management of single IUFD in MC pregnancies remains unknown. Immediate delivery of the surviving twin in this circumstance may not prevent the occurrence of neurological complications [15]. Gestational age appears to be a logical guide to the decision on delivery. If it is remote from term, expectant management with close maternal and fetal surveillance is advised. If neonatal survival is likely, immediate delivery might be a better option to avoid any possible late co-twin sequelae, although some early damage might have already occurred. Neonatal cranial ultrasound is recommended after delivery.

iii. Twin reversed arterial perfusion sequence

The choice of treatment for TRAP depends on the size and growth of the acardiac twin and the cardiovascular status of the pump twin.

Acardiac anomaly in one of the twins, also known as twin reversed arterial perfusion sequence (TRAP), is a rare complication unique to MC pregnancies. The reported incidence is 1 in 100 MC twins and 1 in 30 monozygotic triplets [18, 19]. The primary malformation is the lack of a well-defined cardiac structure in one twin (the acardiac twin), which is kept alive by its structurally normal co-twin (the pump twin) through a superficial artery-to-artery placental anastomosis [18]. The perinatal mortality of the pump twin is over 50%, mainly due to high output heart failure or preterm birth [19]. The diagnosis is by ultrasound. Care must be taken in not mistaking TRAP as single missed abortion in a multiple pregnancy and colour Doppler should help in establishing the correct diagnosis. Treatment modalities include conservative treatment with ultrasound surveillance, medical treatment for heart failure of pump twin, interruption of the vascular connection by intrafetal ablation and cord occlusion. The choice depends on the prognostic indicators, including the size and growth of the acardiac twin and the cardiovascular status of the pump twin [20].

c. Monochorionic monoamniotic (MCMA) twins:

Monoamniotic twining occurs in only 1% of monozygotic twins but is associated with 10-20 % of perinatal mortality [21, 22]. In addition to problems related to MC pregnancies, this type of twining is also associated with specific complications, including conjoined twins and cord accident secondary to cord entanglement.

i. Conjoined twins

Accurate prenatal diagnosis of conjoined twins by ultrasonography is possible in the first trimester.

Conjoined twins are a rare complication of monoamniotic twining, with an incidence of around 1: 55,000 pregnancies [23]. Accurate prenatal diagnosis is possible in the first trimester and allows better counseling of the parents regarding the management options. Sonographic findings include features of monoamnionicity, inseparable fetal bodies and skin contours, and an unchanged relative position of the fetuses [24]. It is also important to note that both false-positive and false-negative cases of conjoined twins have been reported when the diagnosis is made before 10 weeks of gestation [25]. Repeated ultrasound examination for confirmation of the diagnosis between 11-14 weeks is advised. The condition carried very poor prognosis [25]. If termination of pregnancy is decided between 18-24 weeks of gestation, hysterotomy may be required as transvaginal evacuation may not be possible [25].

iii. Cord entanglement and sudden intrauterine death

Ultrasound diagnosis of cord entanglement and close fetal surveillance may help to improve perinatal outcome.

Cord entanglement occurs in over 70% of MCMA twins and is believed to be the major cause for sudden IUFD [26]. Data from case series and retrospective analysis suggests that close antenatal surveillance with ultrasound and cardiotocography from 24 weeks onwards may improve survival in monoamniotic twins [22, 27, 28]. Although cord accident appears unpredictable, it has been suggested that close fetal surveillance might help to detect sub-acute cord accident and hence timely intervention could be instituted to result in better perinatal outcome [22]. Because of the high perinatal mortality, prophylactic delivery by caesarean section at 32 to 34 weeks is recommended [27, 28].

3 TIMING OF DELIVERY FOR UNCOMPLICATED MULTIPLE PREGNANCIES

Delivery should be considered at 38 and 34-36 weeks of gestation for twins and triplets respectively if still not delivered by then.

The perinatal mortality for twin pregnancies starts to rise at 37-38 completed weeks of gestation, compared with 40-41 weeks in singletons [29, 30]. By 39 weeks, the prospective risk of fetal death in twins also outweighs the risk of neonatal death [30]. Therefore, for uncomplicated twin pregnancies, delivery should be considered at 38 completed weeks of gestation if there is no onset of labour. Similarly, the prospective risk of fetal death in triplets exceeds the risk of neonatal death at 36 weeks [30]. It is generally considered appropriate to deliver triplets between 34- 36 weeks since the fetal lung is rather mature and the huge gravid uterus usually causes significant maternal discomforts by this gestation.

4 MODE OF DELIVERY

a. Twins

Vaginal delivery is an appropriate mode of delivery for uncomplicated twin pregnancies with the first twin in vertex presentation.

Planned caesarean delivery for twin is a common practice as a result of a concern on the risk of vaginal delivery for twin pregnancies, especially for the second twin. However, there is yet no evidence to confirm its benefits over vaginal delivery in otherwise uncomplicated twin pregnancies [31]. Vaginal delivery is an appropriate mode of delivery, provided the first twin is in vertex presentation and there is no major obstetric complication. Non-vertex presentation of the second twin before labour should not be a contraindication for vaginal delivery [32, 33].

Current data are insufficient to determine the best mode of delivery if the first twin is in breech presentation. It is the consensus of the Working Group of this guideline that Caesarean section is preferred, on balancing the potential risks of vaginal breech delivery

of the first twin, risks of the second twin in general, the possibility of 'locked twins', and the safety of caesarean delivery in modern obstetrics. 'Locked twins' is exceedingly rare, with a reported incidence of 1 in 817 twin pregnancies [34], but its associated high mortality is a serious concern. Successful vaginal deliveries of breech first twin with good neonatal outcome have been reported [35] and therefore, a trial of vaginal delivery is an option. Women with breech first twin should be adequately counseled the potential risks of each mode of delivery and guided towards a final decision.

b. Triplets and higher-order multiple pregnancies

Caesarean section is usually preferred for triplets and higher-order multiple pregnancies.

The data regarding the optimal mode of delivery in triplets and higher order pregnancies is even more limited. Successful vaginal delivery of triplets has been reported [36]. However, the number of cases is too small for concluding on its safety. The concern includes the difficulty with intrapartum simultaneous fetal monitoring, the unpredictability of the presentation of the remaining triplets after the delivery of the first one, and the potential risks of cord prolapse, abruption placenta and fetal obstruction. Caesarean section is usually preferred for triplet and higher-order multiple pregnancies.

5 INTRAPARTUM MANAGEMENT FOR VAGINAL DELIVERIES OF TWINS

a. First stage

Good intrapartum care includes blood preparation, intravenous access, continuous fetal heart monitoring, adequate analgesia and careful monitoring of the labour progress.

When vaginal delivery is planned, several precautions must be taken. First, maternal blood should be collected for haemoglobin level, typing and screening. Second, intravenous access with a large-bore indwelling catheter should be in place during labour. Third, the management team should consist of obstetrician, anaesthetist, neonataologist and midwives. Lastly, it is also preferable to have an ultrasound machine in the delivery suite for detecting the fetal heart pulsation, fetal lie and presentation when needed.

Both twins should be continuously monitored with cardiotocography throughout labour. To allow separate recordings of the fetal heart rates, the first twin is preferably monitored with fetal scalp electrode while the second one with transabdominal detector.

Adequate analgesia is important for the optimum intrapartum management of twin pregnancies. Epidural analgesia should be considered since it provides not only excellent relief of labour pain, but also analgesia for any necessary manipulation at the second stage of labour, especially if the second twin is in non-vertex presentation.

The progress of labour should be closely monitored with 2-4 hourly vaginal examination. The criteria for diagnosing slow progress are the same as in singletons. In case of inefficient uterine contractions, oxytocin augmentation can be used. Twin pregnancy has no adverse impact on the effectiveness of oxytocin augmentation of labour [37].

b. Second stage

Obstetricians attending the delivery should be experienced with vaginal twin deliveries and skilled in evaluation of fetal position and in intrauterine manipulation.

An experienced obstetrician must be present during the second stage of labour. Following delivery of the first twin, syntometrine must NOT be given as it might facilitate the premature placental separation before the delivery of the second twin. The cord of the first twin should be clamped and divided as usual.

Immediately following delivery of the first twin, the obstetrician should ascertain the lie and presentation of the second twin, using ultrasound if required. Once a cephalic presentation is confirmed, the decent of the fetal head is expected with re-establishment of uterine contractions. Oxytocin infusion should be commenced if uterine contractions have failed to resume. Fetal heart rate should be continuously monitored. Once the head of the second twin is engaged in the pelvic brim, amniotomy can be performed. A twin-to-twin delivery interval

of ≤ 30 minutes is considered an appropriate time, after which delivery should be expedited, since the risks of both acidosis and second stage Caesarean section increase with the length of this interval [38, 39].

If the second twin is in non-vertex presentation, the available options include assisted vaginal breech delivery or breech extraction (if it is breech), internal podalic version following by breech extraction, external cephalic version (ECV) followed by vaginal cephalic delivery, and emergency second stage caesarean section. A systematic review showed that breech extraction has a higher success rate (98% versus 58%) and low fetal distress rate (0.5% versus 18%) compared with ECV [40]. On the other hand, good success rates of up to 70% have been reported in ECV [41]. The choice obviously depends on individual obstetricians' experience. Emergency second stage caesarean section is associated with significant maternal morbidity and should be reserved for cases where vaginal deliveries are thought to be not possible.

c. Third stage

Multiple pregnancies are at increased risks of primary postpartum haemorrhage.

Following the delivery of the shoulder of the second twin, active management of the third stage should ensue. Oxytocin infusion in addition to a bolus of oxytocin is advised as there is an increased risk of primary post-partum haemorrhage. It is advisable to have umbilical arterial cord blood taken routinely from both twins for blood gas analysis. It is particularly important when there is clinical suspicion of fetal distress or birth asphyxia. The placentas should be examined as a routine to confirm the chorionicity and amnionicity.

6 DELAYED INTERVAL DELIVERY OF THE SECOND TWIN IN VERY PRETERM GESTATION

The best management on delivery of the second twin in very preterm gestation is unknown.

In very rare circumstances, the uterine contractions may subside after delivery of the first twin in very preterm gestation (usually < 24 weeks), leaving the second twin in-utero [42]. Further delay in delivery of the second twin might improve the survival chance but might also put the mother at risk of infectious morbidity. Intrauterine infection is also a risk factor for poor perinatal outcome among preterm infants [43]. There are case reports or small case series on successful delay in delivery of the second twin using broad spectrum antibiotics, tocolysis, antenatal corticosteroids or even cervical cerclage under these circumstances [44-46]. However, given the paucity of data, the best protocol for this rare condition still cannot be concluded. Women who are candidates for delayed interval delivery of the second twin should be adequately counseled the risks of such attempt (maternal sepsis, intrauterine infection, chance of failure) and the possible benefit (prolongation of pregnancy).

7 SUMMARY OF KEY POINTS FOR PART II OF THE GUIDELINES

- The indication for delivery of DC pregnancies with discordant fetal growth should take into consideration of the fetal well-being(s), the gestational age and serial growth velocity.
- In MC pregnancies, single IUFD poses a significant risk to the surviving co-twin, mainly due to acute hypotensive episode at the time of the fetal demise. There is no such concern for single IUFD in DC pregnancies.
- MC pregnancies should be monitored closely with ultrasonography for development of TTTS. Fetoscopic laser surgery should be the first-line treatment for severe TTTS diagnosed before 26 weeks of gestation.
- For otherwise uncomplicated twin and triplet pregnancies, delivery should be considered at 38 and 34-36 weeks of gestation respectively.
- Vaginal delivery is an appropriate mode of delivery for uncomplicated twin pregnancies with the first twin in vertex presentation. Caesarean section is preferred for non-vertex first twins, triplets and higher-order multiple pregnancies.
- For vaginal twin delivery, the management team should consist of an experienced obstetrician, anaesthetist, neonataologist and midwives.

REFERENCE LIST

1. Ayres A, Johnson TR. Management of multiple pregnancy: prenatal care--part II. Obstet Gynecol Surv 2005; 60:538-49.

2. Hollier LM, McIntire DD, Leveno KJ. Outcome of twin pregnancies according to intrapair birth weight differences. Obstet Gynecol 1999; 94:1006-10.

3. Saito K, Ohtsu Y, Amano K, Nishijima M. Perinatal outcome and management of single fetal death in twin pregnancy: a case series and review. J Perinat Med 1999; 27:473-7.

4. Petersen IR, Nyholm HC. Multiple pregnancies with single intrauterine demise. Description of twenty-eight pregnancies. Acta Obstet Gynecol Scand 1999; 78:202-6.

5. Robyr R, Quarello E, Ville Y. Management of fetofetal transfusion syndrome. Prenat Diagn 2005; 25:786-95.

6. Denbow ML, Cox P, Taylor M, Hammal DM, Fisk NM. Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. Am J Obstet Gynecol 2000; 182:417-26.

7. Gonsoulin W, Moise KJ, Jr., Kirshon B, Cotton DB, Wheeler JM, Carpenter RJ, Jr. Outcome of twin-twin transfusion diagnosed before 28 weeks of gestation. Obstet Gynecol 1990; 75:214-6.

8. Sebire NJ, Souka A, Skentou H, Geerts L, Nicolaides KH. Early prediction of severe twin-to-twin transfusion syndrome. Hum Reprod 2000; 15:2008-10.

9. Haverkamp F, Lex C, Hanisch C, Fahnenstich H, Zerres K. Neurodevelopmental risks in twin-to-twin transfusion syndrome: preliminary findings. Eur J Paediatr Neurol 2001; 5:21-7.

10. Huber A, Hecher K. How can we diagnose and manage twin-twin transfusion syndrome? Best Pract Res Clin Obstet Gynaecol 2004; 18:543-56.

11. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. N Engl J Med 2004; 351:136-44.

12. Sebire NJ, D'Ercole C, Carvelho M, Sepulveda W, Nicolaides KH. Inter-twin membrane folding in monochorionic pregnancies. Ultrasound Obstet Gynecol 1998; 11:324-7.

13. Sebire NJ, D'Ercole C, Soares W, Nayar R, Nicolaides KH. Intertwin disparity in fetal size in monochorionic and dichorionic pregnancies. Obstet Gynecol 1998; 91:82-5.

14. Hecher K, Diehl W, Zikulnig L, Vetter M, Hackeloer BJ. Endoscopic laser coagulation of placental anastomoses in 200 pregnancies with severe mid-trimester twin-to-twin transfusion syndrome. Eur J Obstet Gynecol Reprod Biol 2000; 92:135-9.

15. Fusi L, Gordon H. Twin pregnancy complicated by single intrauterine death. Problems and outcome with conservative management. Br J Obstet Gynaecol 1990; 97:511-6.

16. Pharoah PO, Adi Y. Consequences of in-utero death in a twin pregnancy. Lancet 2000; 355:1597-602.

17. Graef C, Ellenrieder B, Hecher K, Hackeloer BJ, Huber A, Bartmann P. Long-term neurodevelopmental outcome of 167 children after intrauterine laser treatment for severe twin-twin transfusion syndrome. Am J Obstet Gynecol 2006; 194:303-8.

18. Van Allen MI, Smith DW, Shepard TH. Twin reversed arterial perfusion (TRAP) sequence: a study of 14 twin pregnancies with acardius. Semin Perinatol 1983; 7:285-93.

19. Moore TR, Gale S, Benirschke K. Perinatal outcome of forty-nine pregnancies complicated by acardiac twinning. Am J Obstet Gynecol 1990; 163:907-12.

20. Wong AE, Sepulveda W. Acardiac anomaly: current issues in prenatal assessment and treatment. Prenat Diagn 2005; 25:796-806.

21. Allen VM, Windrim R, Barrett J, Ohlsson A. Management of monoamniotic twin pregnancies: a case series and systematic review of the literature. BJOG 2001; 108:931-6.

22. Heyborne KD, Porreco RP, Garite TJ, Phair K, Abril D. Improved perinatal survival of monoamniotic twins with intensive inpatient monitoring. Am J Obstet Gynecol 2005; 192:96-101.

23. Spitz L. Conjoined twins. Prenat Diagn 2005; 25:814-9.

24. Barth RA, Filly RA, Goldberg JD, Moore P, Silverman NH. Conjoined twins: prenatal diagnosis and assessment of associated malformations. Radiology 1990; 177:201-7.

25. Pajkrt E, Jauniaux E. First-trimester diagnosis of conjoined twins. Prenat Diagn 2005; 25:820-6.

26. Overton TG, Denbow ML, Duncan KR, Fisk NM. First-trimester cord entanglement in monoamniotic twins. Ultrasound Obstet Gynecol 1999; 13:140-2.

27. Shveiky D, Ezra Y, Schenker JG, Rojansky N. Monoamniotic twins: an update on antenatal diagnosis and treatment. J Matern Fetal Neonatal Med 2004; 16:180-6.

28. Rodis JF, McIlveen PF, Egan JF, Borgida AF, Turner GW, Campbell WA. Monoamniotic twins: improved perinatal survival with accurate prenatal diagnosis and antenatal fetal surveillance. Am J Obstet Gynecol 1997; 177:1046-9.

29. Minakami H, Sato I. Reestimating date of delivery in multifetal pregnancies. JAMA 1996; 275:1432-4.

30. Kahn B, Lumey LH, Zybert PA, et al. Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. Obstet Gynecol 2003; 102:685-92.

31. Hogle KL, Hutton EK, McBrien KA, Barrett JF, Hannah ME. Cesarean delivery for twins: a systematic review and meta-analysis. Am J Obstet Gynecol 2003; 188:220-7.

32. Rabinovici J, Barkai G, Reichman B, Serr DM, Mashiach S. Randomized management of the second nonvertex twin: vaginal delivery or cesarean section. Am J Obstet Gynecol 1987; 156:52-6.

33. Caukwell S, Murphy DJ. The effect of mode of delivery and gestational age on neonatal outcome of the non-cephalic- presenting second twin. Am J Obstet Gynecol 2002; 187:1356-61.

34. Cohen M, Kohl SG, Rosenthal AH. Fetal Interlocking Complicating Twin Gestation. Am J Obstet Gynecol 1965; 91:407-12.

35. Blickstein I, Goldman RD, Kupferminc M. Delivery of breech first twins: a multicenter retrospective study. Obstet Gynecol 2000; 95:37-42.

36. Alamia V, Jr., Royek AB, Jaekle RK, Meyer BA. Preliminary experience with a prospective protocol for planned vaginal delivery of triplet gestations. Am J Obstet Gynecol 1998; 179:1133-5.

37. Fausett MB, Barth WH, Jr., Yoder BA, Satin AJ. Oxytocin labor stimulation of twin gestations: effective and efficient. Obstet Gynecol 1997; 90:202-4.

38. Leung TY, Tam WH, Leung TN, Lok IH, Lau TK. Effect of twin-to-twin delivery interval on umbilical cord blood gas in the second twins. BJOG 2002; 109:63-7.

39. Persad VL, Baskett TF, O'Connell CM, Scott HM. Combined vaginal-cesarean delivery of twin pregnancies. Obstet Gynecol 2001; 98:1032-7.

40. Robinson C, Chauhan SP. Intrapartum management of twins. Clin Obstet Gynecol 2004; 47:248-62.

41. Chervenak FA, Johnson RE, Berkowitz RL, Hobbins JC. Intrapartum external version of the second twin. Obstet Gynecol 1983; 62:160-5.

42. Livingston JC, Livingston LW, Ramsey R, Sibai BM. Second-trimester asynchronous multifetal delivery results in poor perinatal outcome. Obstet Gynecol 2004; 103:77-81.

43. Viscardi RM, Muhumuza CK, Rodriguez A, et al. Inflammatory markers in intrauterine and fetal blood and cerebrospinal fluid compartments are associated with adverse pulmonary and neurologic outcomes in preterm infants. Pediatr Res 2004; 55:1009-17.

44. Van der Straeten FM, De Ketelaere K, Temmerman M. Delayed interval delivery in multiple pregnancies. Eur J Obstet Gynecol Reprod Biol 2001; 99:85-9.

45. Hamersley SL, Coleman SK, Bergauer NK, Bartholomew LM, Pinckert TL. Delayed-interval delivery in twin pregnancies. J Reprod Med 2002; 47:125-30.

46. Zhang J, Johnson CD, Hoffman M. Cervical cerclage in delayed interval delivery in a multifetal pregnancy: a review of seven case series. Eur J Obstet Gynecol Reprod Biol 2003; 108:126-30.

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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.