Multiple pregnancies are often impacted by conditions that can lead to preterm delivery and thus high morbidity and mortality of the neonates involved. In 2006, approximately 60% of twins and 92.6% of triplets were born before 37 weeks gestational age. Perinatal mortality rates in developed countries range from 47 to 120 per 1000 births for twins and 93 to 203 per 1000 births for triplets.

Morbidities associated with prematurity include respiratory failure, pneumonia, congenital malformations, necrotizing enterocolitis, intraventricular hemorrhage and retinopathy of prematurity, as well as long term deficits such as cerebral palsy and neurological and motor dysfunction. Multifetal pregnancy also exposes the mother to increased risk of preeclampsia, placental abruption, post-partum hemorrhage, gestational hypertension and operative delivery among other obstetrical complications.

The developed world, including Canada, has experienced a dramatic increase in the number of twin pregnancies. There has been a 35% increase in the birth of twins since 1974. Advanced maternal age, low maternal age, as well as the use of assisted reproductive technologies (ART) have contributed to this rise. One theory as to why older mothers are likely to experience multifetal pregnancies is that advanced maternal age is associated with increased levels of circulating follicle stimulating hormone (FSH) resulting in multiple ovulations due to multiple follicle growth. In addition, ART often involves the implantation of more than one blastocyst in the uterus with the intention of a singleton pregnancy. However, more than one blastocyst may survive.

A delayed-interval delivery is indicated when it is believed the delayed arrival of the second twin will improve its outcome. Neonatal survival after preterm delivery correlates directly with the number of days in utero from gestational ages 23 through 28 weeks. If the birth of the first twin leads to the delivery of the second twin, it contributes to perinatal morbidity and mortality. Survival to discharge of twins after delivery at 22-23, 24, and 25 weeks are 11%, 23%, and 51%, respectively. At such extremes of viability, even small gains in gestation can have significant impacts on survival. Roman et al. reported neonatal outcomes among 16 retained fetuses who survived their NICU.
stay post delivery of twin A at 16w3d to 25w5d. The associated neonatal morbidity included respiratory distress syndrome (75%), major infection (37.5%), bronchopulmonary dysplasia (12.5%) and 37.5% of the neonates actually survived without major morbidity. There were no cases of necrotizing enterocolitis or grade III/IV intracranial hemorrhage.\(^1\) Indeed, the survival rate increases markedly for neonates born from 22-25 weeks gestational age. Data suggests that of neonates born between 23-25 weeks gestational age, 40% will have a normal neurodevelopmental outcome. At 25 weeks gestational age, there is an 80% chance of survival with a NICU admission.\(^13\) Farkouh et al. demonstrated that the retained twin had a shorter hospital admission with a mean length of stay of 47 days compared to 86 days for the first born twin in their study.\(^14\)

However, there are several contraindications to delayed-interval delivery, which must be respected. Gestational age beyond 30 weeks generally has positive outcomes and, therefore, does not necessitate the need to delay delivery. Monochorionicity is contraindicated as vascular anastomosis in the retained placenta may increase the risk of complications, however, it has been performed successfully.\(^15\) Severe preeclampsia, placental abruption and chorioamnionitis of the retained twin all have significant maternal and fetal risks. Additionally, caesarean section of the firstborn or other obstetrical indications for the delivery of all fetuses are also contraindications. However, selective hysterotomy of twin A with successful outcome in twin B has been described.\(^12,16\) Oleyese et al. described that delayed delivery of twin B when the twin A is born at 24 weeks or later had no benefit to reducing mortality. The cohort study demonstrated that there was only a decrease in perinatal and infant mortality when twin A delivered at 22-23 weeks and when the delay interval was 3 weeks or less. Furthermore, delay intervals of 4 weeks or more were associated with a higher risk of small-for-gestational age birth in twin B, regardless of the gestational age of twin A.\(^15\)

A large case series of 200 twin pregnancies in the United States from 1995-1998 described delayed-interval deliveries of the first twin born at 17-29 weeks with a mean delay of 6 days (range of 2-107 days). Delayed-interval delivery of twins compared to non-delayed twins at the same gestational age had a 1-year survival rate of 56% compared to 24% for non-delayed twins. The case series concluded that delayed-interval deliveries could improve infant survival and reduce neonatal morbidity.\(^17\)

Although slight intervals between the deliveries of siblings during critical gestational ages of less than 30 weeks can achieve clinically significant benefits and decrease both neonatal morbidity and mortality, the choice to do so should be up to the patient. Extending the gestation of the second sibling from previable to perivable age will reduce mortality, but it may also result in the risk of long-term morbidity due to prematurity. Therefore, the option to deliver both twins at the same age and time, with the risk of mortality, should be made available to the patient after significant discussion of risks and benefits.\(^16\) The critical period of perinatal morbidity and mortality is between weeks 23 and 28 of gestation.\(^8\)

**Case**

A 37-year old G2P0 with dichorionic diamniotic twin pregnancy resulting from IVF presented at 23w2d to a high risk obstetrics centre after experiencing previous preterm premature rupture of membranes of twin A at 19 weeks gestation with persistent oligohydramnios. The ultrasound examination revealed cephalic presentation for twin A with transverse presentation for twin B. The patient had a remote history of anterior uterine fibroids for which she received a hysteroscopic myomectomy and was Group B Streptococcus negative.

The patient was treated with two doses of betamethasone at 23w4d and 23w5d and nifedipine at 25w5d for tocolysis due to extreme prematurity, during which she experienced a new onset of vaginal bleeding. At 25w6d she received MgSO\(_4\) for neuroprotection as she was felt to be in preterm labour. At 26w1d, twin A showed variable decelerations, and delayed interval delivery was presented as an option to the patient versus delivery of both fetuses at the same time. After extensive review of the literature and discussion of the maternal and neonatal risks and possible benefits, the decision to attempt the delayed interval delivery was agreed upon by the patient, her partner and the Maternal Fetal Medicine Department. The patient was afebrile, white blood count (WBC) was normal, and discharge was normal with no evidence of chorioamnionitis. Consequently, a spontaneous vertex delivery of a live male weighing 740 g with Apgar scores of 4, 5, 7 after 1, 5 and 10 minutes respectively, occurred in the operating room. The umbilical cord of twin A was clamped with two Endoloop PDS sutures and was cut close to the placenta. Nitroglycerine 200 μg IV was administered in addition to IV gentamicin and IV clindamycin as per recommendations in the literature search as nitroglycerine promptly initiates uterine quiescence. The lower uterine segment was then irrigated with 50 000 units of bacitracin in 1 L of normal sterile saline, 700 cc of which was flushed into the lower uterine segment through a 16 French Foley catheter.
Following delivery of twin A, ultrasound examination of twin B revealed a normal fetal heart rate (FHR) and cord presentation. The PDS suture was visible on ultrasound and twin B was in transverse presentation. The patient was observed in the operating room with continuous electronic fetal monitoring for one hour. She was then started on indomethacin 100 mg PR for 48 hours and IV gentamicin and clindamycin was continued for 72 hours.

At 26w2d, transvaginal ultrasound exam revealed a 3.2 cm long cervix and normal amniotic fluid volume around twin B (Figure 1). The interval delivery was delayed subsequently for 8 days. The delay period included daily CBC with C-reactive protein (CRP), fetal non-stress tests three times per day, broad-spectrum antibiotics for 7 days and tocolytics for 48 hours.

At 27w1d the patient was assessed for increased contractions every four to five minutes and a temperature of 37.7 °C. The patient had no loss of fluid or vaginal bleeding and FHR was normal. The pelvic exam demonstrated a closed cervix. One day later, blood and urine cultures were taken and IV gentamicin and clindamycin were restarted. The patient's temperature was 37.8 °C and heart rate was 120 bpm, while the FHR was 150-160 bpm with moderate variability. With WBC 15.98 x 10^9 L^-1, hemoglobin 10 g L^-1, platelets 280 x 10^9 L^-1, a diagnosis of chorioamnionitis was made. This resulted in delivery via low transverse caesarean section at 27w2d for breech presentation. A live male infant weighing 1100 g was delivered with Apgar scores of 6 and 8 at one and five minutes, respectively, with no signs of infection.

Pathology review revealed placenta A had focal acute funisitis and mild acute subchorionitis while placenta B had minimal focal acute phlebitis.

Post partum, the patient’s WBC decreased to 10.91 x 10^9 L^-1, hemoglobin 84 g/L and both blood and urine cultures remained negative. The maternal post partum course was uneventful and she remained in hospital to care for her twins. Twin A initially required high frequency ventilation, then went onto conventional ventilation with low oxygen fraction for respiratory support. Twin B was initially intubated for surfactant administration, but quickly went onto continuous positive airway pressure. Both twins are currently in excellent condition and have returned home.

Discussion

While there are no guidelines regarding management following delivery of the first twin, high ligation of the umbilical cord with the placenta left in-situ is recommended. It is suggested that the umbilical cord be tied with absorptive suture close to the placenta. This allows the cord stump to be cut away from the placenta, which is thought to reduce the risk of chorioamnionitis. An Endoloop allows the suture to be placed higher in the birth canal, well above the internal os.

Bacitracin 50 000 U/L can then be applied to the lower uterine segment to reduce infection risk. It is important to monitor the presence of fever, leukocytosis and elevated CRP, as such markers may be indicative of chorioamnionitis. It is also recommended that ultrasonography is used to assess cervical dilation and length as digital pelvic examination can increase the risk of chorioamnionitis.

Some study protocols suggest cervical cerclage after a seven day delay interval as silent cervical dilatation may be implicated in the preterm birth of twin A in the first place. Cerclage can minimize fetal membrane exposure to vaginal flora and low pH. However, the placement of a cerclage prior to the decision to delay a delivery results in poorer outcomes, often due to intra-amniotic infection, or rupture of membranes. Indeed, previous cerclage may even decrease the latency period, or period of delay between births, compared to a woman who has never had a cerclage. Cerclage may also be discouraged due to the possibility of increased risk of chorioamnionitis.

The administration of tocolytics, in addition to broad-spectrum antibiotics, are also important interventions to consider when planning to delay the birth of a second fetus. Indeed, intra-amniotic infection is a common cause of failure to prolong pregnancy, as women who have intrauterine infection do not respond as well to tocolytic therapy.

Many studies to date that report on outcomes of delayed-interval deliveries involved either case series or case reports. One review discussed the importance of delayed-interval deliveries that took the second sibling past the 24th week, or the week of viability. Of such

![Figure 1](image-url)
Delayed-interval pregnancy

cases, 24/70 neonates survived and the range of latency was 3-143 days, with a mean latency of 44.8 days. Of the delayed deliveries that resulted in neonatal viability, the mean latency period was 57.5 days. However, delayed deliveries resulting in neonatal death corresponded to a mean latency of only 17.3 days.6

Maternal morbidity and mortality is also a primary concern with delayed-interval deliveries. A retrospective review of 5 sets of twins and 2 sets of triplets demonstrated that the duration of maternal hospital admission was directly correlated to length of delay between deliveries. This meant that the length of hospital admission was related to the prolonged antepartum course and not the post-partum stay due to possible maternal morbidity. Of the patients in the study, four experienced intra-amniotic infection and one had a case of maternal sepsis, which was treated with broad-spectrum antibiotics. There were no maternal deaths described.23 Another retrospective review referenced a patient who required a postpartum hysterectomy as a result of hemorrhage, uterine atony and myometrial micro-abscesses on pathology. The study also described a 31.6% incidence of serious maternal morbidity.12 Arabin and colleagues discuss the risks of chorioamnionitis (24%), placental abruption (5%), post partum hemorrhage (11%) and manual removal of placental contents (11%). They also describe a case of delayed interval delivery of triplets where the mother became septic from pyelonephritis. Furthermore, one patient went into transient atrial fibrillation without sequelae and another required an appendectomy three days post partum.22

Conclusion

Delayed-interval delivery provides an opportunity to increase the chance of survival of the second fetus in situations where the first is born too soon (<30 weeks). Although there are no consensus guidelines on this approach, many case reports have suggested options that have provided positive outcomes that reduce neonatal morbidity and mortality.

It is paramount to ensure there are no signs of infection in the mother or fetuses before delay is considered and a thorough informed consent process must be undertaken as there is no robust research to support immediate delivery versus delayed interval delivery.

Acknowledgements

The patient whose case is presented has provided signed permission for its publication.

References