

Cervical cerclage or not in delayed delivery interval: obstetric management and outcomes

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Research

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Abstract

Objective

The aim of this study is to explore the effectiveness of cervical cerclage in order to delay the delivery interval after delivery of the first fetus in dichorionic twin pregnancies.

Study Design:

Records of 11 twin pregnancies where delayed delivery was experienced for retained fetus(es), were collected retrospectively. Cases with cervical cerclage placed after the first delivery were evaluated as the cerclage group and cases without cerclage placement were evaluated as the non-cerclage group.

Results

The median duration of the delay 25.4 ± 8.1 days (range, 4–50) in the cerclage group and 7.7 ± 2.0 days (range, 3–17) in the non-cerclage group ($P = 0.045$). Average gain birthweight of the second fetus in the cerclage group was 408.0 ± 160.2 g and 93.3 ± 25.5 g in the non-cerclage group ($P = 0.061$). But other parameters were not different between the two groups.

Conclusions

Cervical cerclage after the first delivery is associated with a longer inter-delivery interval without increasing the risk of intrauterine infection.

Introduction

Multiple pregnancies are increasing significantly due to the vigorous expansion of assisted reproductive technology (ART) in recent decades [1]. Multiple gestations are associated with severe antenatal complications such as threatened preterm labor, preterm rupture of membranes and birth defects. These conditions have resulted in a severe increase in morbidity and mortality rates, which have brought great challenges to perinatal care[2].

Delayed interval delivery is defined as every attempt to postpone parturition of the second twin by at least performing in utero percutaneous umbilical cord ligation and extending delivery by at least 24 hours [3]. It has been reported that this method can significantly prolong the gestation of the second fetus and improve its survival odds and general fetal outcome in the recent years [4–6]. However, premature delivery of the first fetus in a twin pregnancy is an antenatal complication for which no consensus has yet been achieved regarding an optimal management protocol [4]. Despite the fact that prolongation of delivery interval is undoubtedly critical with regards to the improvement of perinatal outcomes of the second fetus, there is a still a dilemma on whether cervical cerclage or other conservative approach is the superior method of

treatment [5–7]. At present, the guideline does not recommended that cervical cerclage is performed for twin gestations, which is believed to be associated with an enhanced rate of premature delivery [8]. However, under special circumstances, it is possible that a twin pregnancy experiences a dilatation of the cervical os and expulsion of a fetus, but the remaining one is left in the uterine cavity. The pathological process differs between singleton and twin pregnancies. The decision to conduct a cerclage intervention rests on the application of existing experimental data of singleton or twin gestations to guide the next diagnosis and treatment. Therefore, it is imperative for us to provide more cases to supplement existing evidence, provide appropriate management and ensure the most favorable outcome.

The aim of the present study is to explore the effectiveness (maternal and fetal outcomes of pregnancies) of cervical cerclage in order to achieve delayed-interval delivery after miscarriage of the first fetus in dichorionic twins.

Methods

Selection of patients

It is a retrospective study that was conducted during the 2016–2020 period in the Department of Obstetrics and Gynecology of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, which belongs to a teaching center that receives a large number of high-risk pregnancies from all over Central China. In this present study, cases of dichorionic twins in which delivery of the first fetus occurred following admission in our department were exclusively included, and data of twin pregnancies with delayed interval delivery were collected. Inclusion criteria included were: (1) diamniotic gestation; (2) uterine contractions subsided after delivery of the first fetus and cervix had contracted; (3) the second fetus exhibited no sign of fetal distress or congenital malformation. Exclusion criteria were as follows: chorioamnionitis, premature rupture of membranes of the second fetus, severe maternal vaginal blood loss, poor maternal general condition, preeclampsia and suspicion of placental abruption.

As a result, a total of 11 twin cases were deemed suitable to be evaluated. Cases with cervical cerclage placement after the first delivery of the clinician and the patient were evaluated as the cerclage group, and the cases where cerclage was not performed were regarded as the non-cerclage group. Medical records of these cases concerning the antenatal and perinatal outcomes were retrieved. The Institutional Review Board (IRB) of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB20180513) has approved of this study protocol.

Tocolytic therapy

Following the admission to our department, all women presenting with symptoms of threatened labor, such as uterine contractions, vaginal bleeding, cervical dilatation and preterm premature rupture of membranes (PPROM), were initially managed with tocolytic therapy. This included hospitalization, iv administration of beta-adrenergic agonist (ritodrine), magnesium sulphate or atosiban or oral intake of nifedipine. In cases who were experiencing contractions or those who would likely develop contractions, doses were gradually increased until contractions could be stopped. In case of PPRM, iv administration of

ampicillin regimen was used for 7 days. Low molecular weight heparin (LMWH) was prescribed in selected cases.

Cervical cerclage treatment and monitoring

In the 11 cases who were found suitable for the trial of delayed interval delivery and who had provided informed consent, the placenta was left in situ after the first delivery. The umbilical cord of the first fetus was sutured with No. 0 non-absorbable suture (Mersilk, Ethicon, Johnson and Johnson company, USA) and cut as deeply as possible at the level of the cervix. After the interruption of uterine contraction and bleeding, cerclage was performed in 5 pregnancies by means of the McDonald's technique using a No. 2 Prolene suture within the first 24 h. Cerclage was not performed in six other pregnancies. After performing cervical cerclage, women were managed by antibiotics and tocolytic treatment. Betamethasone was routinely injected intramuscularly at 12 mg/day for 2 days to all patients who had completed 26 weeks of pregnancy. Low molecular weight heparin was used in the presence of obesity, known history of thrombophilia, and if long-term bedrest were to be recommended to the patient.

The cultures taken after childbirth (vaginal, endocervical and urine) and the laboratory tests (blood routine and other infection index) by 3-day intervals were regularly monitored as follow-up studies. Follow-up of fetal well-being was evaluated by external monitoring, and cervical length was determined by performing weekly transvaginal cervical length measurements.

Clinical characteristics

The following clinical data were collected from the medical records of each patient: age, parity, gravidity, history of previous miscarriages and the method of conception of the present pregnancy were obtained. Obstetric parameters such as cause of first delivery (PPROM, preterm labor at admission), gestational week at admission, neonatal outcomes of the first and second twin such as gestational age at delivery, neonatal birth weight, Apgar score in the first and fifth minute of neonatal life, admission to the Neonatal Intensive Care Unit (NICU) and the viability of neonates after 1 month of life, cervical dilatation, delivery interval (interval between the delivery of the first and second twin) were analyzed. In addition, maternal complications, such as postpartum hemorrhage, placental implantation and chorioamnionitis, as well as the number of take-home babies and follow-up results of the neonates were also recorded.

Statistical analysis

Statistical analyses of the frequency data and continuous variables were performed using Mann-Whitney U-test and χ^2 -test method. A p-value of less than 0.05 was considered significant. SPSS 17.0 (SPSS Inc., Chicago, IL) was used for all statistical analysis.

Results

Delayed delivery prolongs the gestation of the second fetus and improves its survival rate

Obstetric and demographic variables of the five twin pregnancies in the cerclage group and the six in the non-cerclage group are summarized in Table 1 and Fig. 1.[Table 1 and Fig. 1 near here] The median age of the expectant mothers was 31.3 ± 1.0 years (range, 25–36). Eight cases were primigravid and three were primiparous. Seven pregnancies were conceived using in vitro fertilization (IVF) technology, two pregnancies were mediated using ovulation induction and two cases became pregnant naturally. Five patients were admitted due to PROM and the other six were because of preterm labor. The mean gestational age at delivery of the first fetus was 22.0 ± 1.1 weeks and the mean birth weight of first fetus was 424.5 ± 103.4 g. Three (27.3%) first neonates were alive and the mean cervical dilatation at admission was 2.19 ± 0.21 cm. Delivery was inevitable when the uterine contractions could not be reversed in spite of tocolytic therapy. The mean gestational age at spontaneous delivery of the second twin was 24.2 ± 1.2 weeks. Eight out of the eleven neonates were born alive (72.7%) and the mean birthweight of the live births was 660.9 ± 133.2 g. The median latency period of the delivery interval was 15.7 ± 4.6 days, while the maximum prolongation of the interval delivery was 50 days. There were four cases of maternal complications of which two were postpartum hemorrhage and placental adhesion, and two were chorioamnionitis. The remaining seven mothers were discharged after delivery without complications.

Table 1
Presentation of the major obstetric characteristics and neonatal outcomes

Case No.	1	2	3	4	5	6	7	8	9	10	11
Ages(years)	34	29	33	32	35	36	28	33	25	28	31
Mode of conception	IVF	NC	IVF	IVF	IVF	IVF	IVF	OI	IVF	OI	NC
The first fetus											
Cause of first delivery	PTL	PP	PP	PTL	PP	PP	PTL	PTL	PTL	PP	PTL
Gestational age(weeks)	21 + 2	18 +6	24 + 5	22 + 3	19 +6	23 +2	24 + 3	29 + 5	19 +3	16 +4	21 +6
Birthweight(g)	300	200	500	380	240	400	500	1400	250	150	350
Apgar score	0	0	2-3	0	0	1-1	1-2	7-8	0	0	0
Neonatal outcome	Died	Died	NICU	Died	Died	Died	Died	NICU	Died	Died	Died
Cervical dilatation(cm)	1.5	2.5	2.1	3.0	1.6	2.6	2.2	3.5	1.5	2.3	1.3
Cervical cerclage	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No
The retained fetus											
Gestational age(weeks)	28 + 3	20 +4	25 + 2	27 + 1	23 +6	24 +2	25 + 1	30 + 6	19 +6	17 +3	23 +3
Birthweight(g)	1200	280	650	1050	480	500	600	1600	280	180	450
Apgar score	3-6	0	2-5	3-7	1-2	2-3	1-2	7-8	0	0	1-1
Neonatal outcome	Died	Died	NICU	NICU	Died	Died	Died	NICU	Died	Died	Died
Interval (days)	50	12	4	33	28	7	5	8	3	6	17
Maternal complications	PH,PI	-	-	-	CA		PH,PI	CA			
Take-home baby number	0	0	1	0	0	0	0	1	0	0	0
Follow-up results	-	-	Well					Well			
PH: postpartum hemorrhage; ,PI: placental implantation; CA: Chorioamnionitis											

PTL: preterm labor; PP: preterm premature rupture of membranes

Perinatal outcomes in cerclage group exceeds that in non-cerclage group

Perinatal outcomes of the cerclage group and non-cerclage group are detailed in Table 2. [Table 2 near here] The overall median duration of delay was 15.7 ± 4.6 days (range, 3–50). It was found to be 25.4 ± 8.1 days (range, 4–50) in the cerclage group and 7.7 ± 2.0 days (range, 3–17) in the non-cerclage group; and the difference between both groups was statistically significant ($P = 0.045$). Average birthweight growth of the second fetus from the cerclage group was 408.0 ± 160.2 g and 93.3 ± 25.5 g in the non-cerclage group ($P = 0.061$). The gestational age at delivery of the second fetus, its birthweight, live birth rate and take-home baby rate were higher in the cerclage cohort than that in non-cerclage group but was not statistically significant ($P > 0.05$).

Table 2
Analysis of obstetric and neonatal outcomes of cerclage and non-cerclage cases

	All cases (n = 11)	Cerclage group (n = 5)	Non-cerclage group (n = 6)	P-value
The first fetus				
Gestational age(weeks)	22	21 + 3	22 + 3	0.822
Birthweight(g)	424.5 ± 103.4	324.0 ± 53.4	508.3 ± 185.0	0.510
Live birth rate	27.3%(3/11)	20%(1/5)	33.3%(2/6)	0.621
The second fetus				
Gestational age(weeks)	24 + 1	25	23 + 4	0.516
Birthweight(g)	660.9 ± 133.2	732.0 ± 172.4	601.7 ± 209.1	0.548
Live birth rate	72.7%(8/11)	80%(4/5)	66.7%(4/6)	0.621
Interval (days)	15.7 ± 4.6	25.4 ± 8.1	7.7 ± 2.0	0.045
Weight growth(g)	236.4 ± 85.4	408.0 ± 160.2	93.3 ± 25.5	0.061
Maternal complications rate	36.4%(4/11)	40%(2/5)	33.3%(2/6)	0.819
Take-home baby rate	18.2%(2/11)	20%(1/5)	16.7%(1/6)	0.887

Complications of the mother and fetuses in the cerclage group and non-cerclage group

Chorioamnionitis was diagnosed in one patient from the cervical cerclage group and one patient from the non-cervical cerclage group and both were discharged in a healthy condition (case 5 and case 8). Postpartum hemorrhage which required 4 units of blood transfusion occurred in two cases due to placental adhesion and

there was no need for hysterectomy in any of the cases. Four cases showed bacterial vaginosis and vaginitis and seven cases showed normal vaginal flora characteristics.

Eight out of eleven newborns were lost due to prematurity and respiratory problems, and one showed favorable outlook until the 37th day when he suffered a sudden deterioration due to pulmonary hemorrhage that precipitated his death in the NICU and his weight at discharge was 1450g. Two newborns remain alive, one of whom is still healthy at 9 months after the delivery and is demonstrating normal psychomotor development. Long-term follow-up results of the other case could not be produced after hospital discharge.

Discussion

Many literature have reported that delayed delivery can significantly prolong the gestation of the second fetus, thereby increasing the birth weight of the latter, and improving its survival rate and general neonatal outcome[4–7]. It has been reported in previous works that interval between the births of both twins could span between 1-141 days and the survival rate following delayed-interval delivery across different clinical centers was 25%-82.6% [9–11]. Arabin's prospective study of 17 years has reported a significant increase in the survival of the second twin (74% versus 34%) with an average interval of 19 days (1-107 days) in twin pregnancies, and no increase in survival for the second/third triplets (25% versus 25%) with an average interval of 18 days (1-118 days) in triplets pregnancies[10]. A multicenter study in France has shown a significant increase in the survival of the second twin (78.6% versus 7.4%) with an average interval of 47 days (3-140 days) in twin pregnancies[12]. This is consistent with the results of this study, which showed that the median latency period of delivery interval was 15.7 ± 4.6 days, the live birth rate increased by 45.4% and neonatal body weight increased by 236.4 ± 85.4 g, which illustrates that delayed delivery can improve the survival rate and fetal outcome.

However, no consensus has yet been achieved concerning the optimal management of twin pregnancies after delivery of the first fetus. Even though it is highly controversial regarding whether the cerclage procedure can prevent preterm delivery in twin pregnancies, it is undoubtedly beneficial for the extension of delayed interval delivery. Therefore, we have retrospectively analyzed the pregnancy outcomes of the cerclage group and the non-cerclage group, and found that the interval of the cerclage group was significantly longer than that of the non-cerclage group (25.4 ± 8.1 vs 7.7 ± 2.0 days, $P = 0.045$), which showed that cervical cerclage is effective for delayed-interval delivery after delivery of the first fetus in dichorionic twins. There have been some published reports exhibiting that cervical cerclage placement for delayed interval delivery has shown a positive effect on the prolongation of the gestation, morbidity and mortality of retained fetuses[6, 13–16]. In the most extensive review evaluating 148 multiple pregnancy cases reported until 2005, it was conveyed that 60% of the cases (58/97) had undergone cerclage intervention, the mean latency interval tended to be longer when compared with non-cervical cerclage group (50 days vs 43 days) [13]. Emek found that cervical cerclage after the first delivery is associated with a longer delivery interval (40 days vs 12 days, $P = 0.003$) and higher birthweight of the retained fetus (850 ± 153.6 g vs 549.5 ± 149.1 g, $P = 0.04$), but live birth rate and take-home baby rate were not significant between cerclage group ($n = 11$) and non-cerclage group ($n = 9$) [6]. Stamatios et al. also supported the beneficial effects of prolonging the delivery interval in five premature dichorionic twin pregnancies after performing

cervical cerclage, the median delivery interval was 72 days and this study's maximum period was 121 days [14]. Zhang et al. conducted a review of seven series of cases and concluded that cervical cerclage could be useful for delayed interval delivery since it significantly lengthens the interval between twins' birth without increasing the rates of intrauterine infection. The median inter-delivery interval was 25 and 8 days in patients with and without cerclage, respectively [15]. Fayad et al. have found a median interval of 61.7 days in cerclage placement group and 39.7 days in the non-cervical cerclage group, and claimed a longer interval between deliveries after cerclage but it was without significant statistical difference ($P = 0.13$) owing to the small number of cases [16]. Likewise, these results are consistent with our findings, all demonstrating that cerclage after the first delivery is associated with a longer inter-delivery interval.

The advantages of cervical cerclage in our opinion are as follows: 1. adequate vaginal disinfection during cerclage can decrease the possibility that fetal membranes encountering bacteria and vaginal acidity to reduce the risk of intrauterine or systemic infection; 2. closing the uterine orifice can reduce exposure of the amniotic sac to the vagina to prevent the risk of premature rupture of the second fetal membranes; 3. Decreasing the mechanical pressure of the fetal head on the cervix can reduce the production of arachidonic acid and avoid uterine contraction and premature delivery of the second fetus; 4. improving cervical function in patients with cervical incompetence. In our study the average cervical dilatation after the first birth was 2.19 ± 0.21 cm and three of the eleven patients even had amniotic sacs protruding from the cervical os. Four cases showed bacterial vaginosis and vaginitis and five patients were initially admitted due to PROM. Therefore, cervical cerclage can reduce the chance of exposure of fetal membranes to vaginal bacteria and acidic environment, thus reducing the incidence of chorioamnionitis and premature rupture of the second fetal membranes in the above patients.

Those who oppose cervical cerclage have argued that cerclage placement may increase infectious complications, such as PPRM, chorioamnionitis, could cause cervical damage or bleeding with its invasive nature, and induce premature delivery [17–18]. However, in this study we have found that cervical cerclage did not increase the risk of infection and there was no significant difference in the risk of chorioamnionitis and premature rupture of the second fetal membranes between cervical cerclage group and non-cerclage group. Emek reported that chorioamnionitis developed in four patients (36.3%) in their cervical cerclage group and one patient suffered sepsis and septic shock, but was discharged in a healthy condition. Chorioamnionitis was observed in three cases (33.3%) in the non-cerclage group and chorioamnionitis ratio were not different in between the groups [6]. Histopathology reports revealed 43% of chorioamnionitis at completed delivery, however, none resulted in severe further maternal infections like sepsis which was pointed out by Zhang (up to 5%) [19]. Two patients (18.2%) had postpartum hemorrhage due to placental adhesion but there were no further complications. In total, the maternal complications were minimal which was in accordance with a recent review. In addition, many people think that cerclage is not effective in the cases of cervical incompetence during twin pregnancies, in spite of the fact that literatures report that cerclage is not recommendable for twin pregnancies, but after the first birth it is equivalent to a singleton pregnancy experiencing cervical incompetence. Related works, as well as our results, all favor that cerclage is beneficial for singleton pregnancy [8].

Therefore, we believe that cervical cerclage is necessary for delayed delivery, but the conditions and timing of cerclage are not detailed in the current literature, and we hence propose that the suitable conditions for cervical cerclage in delayed delivery be as follows: 1. uterine contraction must subside after the first birth; 2. the second fetus exhibits no sign of fetal distress or congenital malformation; 3. cervical dilatation (CL < 2.5cm) with or without protrusion of the amniotic sac; and 4. no premature rupture of the second fetal membranes, chorioamnionitis, severe vaginal bleeding, suspicion of placental abruption and maternal comorbidities after the first fetus' delivery. There is no uniform standard for the timing of cerclage at present, Cristinelli reported 48 cases had undergone the procedure immediately after the first delivery and 10 cases in 72 h to 10 days later [13]. It is believed that the best time is within 24–72 hours. If there is no uterine contraction or rupture of membranes, cerclage is feasible. The specific method of cervical cerclage can be transvaginal operation, which has various methods of surgical techniques, such as Shirodkar method, McDonald suture method, Cautifaris method, and so on. The surgeon should decide the most suitable way according to his own experience and proficiency. However, in our study the McDonald cervical cerclage approach was used mostly due to its simplicity, security and effectiveness. Antibiotics and uterine contraction inhibitors are recommended after operation. Close antenatal surveillance of both mother and fetus is strongly suggested among these special cases. Routine performance of amniocentesis for the evaluation of the amniotic fluid for inflammatory markers and routine cultures can be performed if necessary [20]. As continuing progress in neonatal care is being made, it was put forward that pregnancy should not exceed 32 weeks due to the enhanced neonatal survival rate and the higher risk of infection and bleeding after 32 weeks of gestation, and therefore cervical cerclage can be removed after this milestone.

Our study is not devoid of limitations. The small number of cases meeting our inclusion criteria in daily clinical practice inevitably limits the sample size of our study. Furthermore, the unavailability of further data concerning the postnatal outcomes of neonates, such as long-term outcome may also be considered as a handicap. This analysis is also limited by its retrospective design. Furthermore, we are aware of a potential selection bias resulting from the experience of the perinatal team available at the time of patient presentation. Nevertheless, our research includes a comparatively satisfying number of cases and indicates the effectiveness of cervical cerclage in prolonging the interval between the delivery of the two fetuses. This represents a reasonable approach for suitable cases in the hand of an experienced team and a standard treatment protocol should be established in the perinatal center. Cervical cerclage is a good recommendation for patients desiring delayed delivery. Therefore, the medical team managing such cases has to keep delayed interval delivery in mind as one potential therapeutic approach in multiple gestation cases subjected to imminent preterm birth.

Conclusion

In the light of the above findings, multiple pregnancies remotely situated from term, delaying the delivery of other fetuses that are retained after the birth of the first one may increase the interval and the surviving chance of the remainder. It is a suitable alternative to the termination of pregnancy. Our results may provide a positive contribution of cervical cerclage to the neonatal outcomes, through the prolongation of delivery interval in dichorionic gestation and this may contribute to the increased birthweight of the newborn. Cervical cerclage is a good treatment alternative for patients wishing for with delayed delivery and it can be removed

after 32 weeks of gestation. Therefore, further prospective studies comparing exclusively conservative treatment with cervical cerclage should be performed in order to achieve more definitive conclusions.

Declarations

Ethics approval and consent to participate

Ethical committee approval was obtained from the Institutional Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB20180513).

Consent for publication

All presentations of case reports consented to publish.

Availability of data and materials

Please contact author for data requests.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NY collected, analyzed and interpreted the data, and drafted the initial version of the manuscript. XG were in charge of the research program on pregnancy complications, have designed the study, assisted with the interpretation of the data and writing of the manuscript.

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Figures

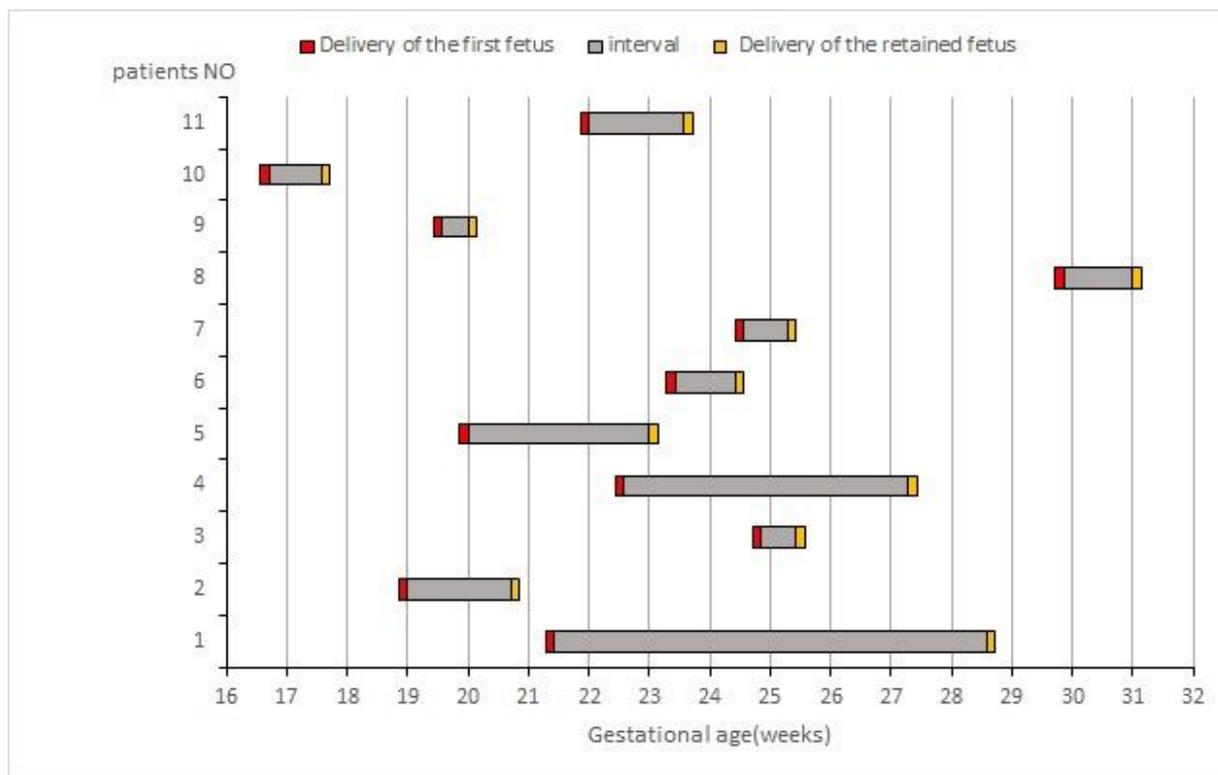


Figure 1

Interval of delayed deliveries in multiple gestations