

# Neonatal and maternal outcomes after intentional delayed delivery for the second twin in dizygotic pregnancy. Case report and literature review

*Prognosticul neonatal și matern în nașterea întârziată intenționat a celui de-al doilea făt din sarcina dizigotică. Caz clinic și revizuirea literaturii*

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## Abstract

Intentional delayed delivery of second twin in dizygotic pregnancy is rare. There are analyzed the peculiarities regarding maternal, short-term neonatal outcomes in a 41-year-old mother, admitted in a tertiary university maternity, diagnosed with: IVG IIP 24 weeks + 3 days dizygotic pregnancy, alive fetuses (A. breech presentation, 690 g, palpable amniotic sac; B. cephalic presentation, intact membranes, EFWs of 690/700 g - ultrasound). At 26 weeks of gestation, after PROM, short positive trial of labor for planned vaginal delivery, under continuous CTG, Bracht maneuver for breech presentation which records the birth of female fetus A, 920 g, Apgar score 5/6. Sectioned umbilical cord is introduced in the vagina. At 50 days of close monitoring and treatment for both mother and fetus B, it is done caesarean section for female fetus B, 1870 g (34 weeks of gestation), Apgar score 8, placenta A/B: 200/450g. Maternal postoperative evolution is normal. Baby A is admitted at Neonatal Intensive Care Unit (NICU) for moderate hypoxia at birth, repeated apnea crisis, without functional respiratory syndrome, anemia being corrected with blood derivatives, 70 days, with gastric-tube nutrition, antibiotics, stage I retinopathy, bilateral hip risk; the weight of fetus B was 1550 g at the cesarean section and 2250 when discharged. Baby B had a favorable evolution (breastfeeding plus formula milk). **Conclusions.** Vaginal delivery at a multipara can be assumed in breech presentation, after a precise protocol, followed by experienced obstetrical/neonatalogical teams, and an intentional delayed CS delivery is feasible. Fetus B is larger at delivery than fetus A at the same moment (1870 g vs. 1550 g), and at discharge (2250 g vs. 2975 g), with a very short admission in NICU/preterm wards. No maternal complication appeared. **Keywords:** intentional delayed delivery, dizygotic pregnancy, preterm delivery, outcome

## Rezumat

Sarcina gemelară dizigotică - cu riscurile și costurile crescute ale mortalității și morbidității perinatale, induse de prematuritate, complicațiile fetale/materne intrapartum - impune decizii dificile pentru terminarea nașterii, dictate de vârsta gestațională, calitățile colului, starea membranelor, prezența și starea feților. Operația cezariană planificată pentru prezența pelviană și monitorizarea CTG intrapartum nu au fost urmate de succesul scontat, ci de discordanța dintre morbiditatea perinatală pe termen scurt și prognosticul neurologic pe termen lung. MG, de 41 de ani, UM 15 mai 2014, internată în 2.11.2014 pentru CUD sistematizate, suspiciune de membrane fisurate, diagnosticată cu: IVG II P, sarcină gemelară dizigotică de 24 săptămâni + 3 zile, feți vii (A. prezența pelviană, 690 g, pungă amniotică palpabilă; B. prezența craniană, 700 g, membrane intacte ecografic). În 17.11.2014 se rup membranele la fătul A, iar după un travaliu de 4 ore se expulzează cu ajutor manual Bracht un făt feminin de 920 g, scor Apgar 5/6, se pensează cordonul, gravida este menținută sub supraveghere/tratament continuu, cu evoluție favorabilă, fără decolarea placentei fătului A, spitalizat la NICU (hipoxie moderată la naștere, adaptare cu crize de apnee, fără sindrom funcțional respirator, anemie plurifactorială, antibioterapie complexă cu spectru larg, gavaj 70 de zile, retinopatie stadiul I, risc bilateral de șold). La 50 de zile de la naștere, la 33 de săptămâni și 4 zile (cronologic, sonografic), se decide extragerea fătului B prin operație cezariană: sex feminin, 1870 g, scor Apgar =8; placenta A de 200 g, placenta B de 450 g. Evoluția post-partum este normală, cu prelungirea spitalizării cu alte 23 de zile, din cauza prematurității fetale. La data operației cezariene fătul A cântărea 1550 g și apoi 2250 g la externare. Fătul B are evoluție favorabilă, cu 2975 g la externare, alimentat mixt (la sân și biberon). **Concluzii.** Monitorizarea extrem de atentă a sarcinii dizigotice, la secundipară, poate permite alegerea nașterii pe cale vaginală a primului făt în prezența pelviană după un protocol precis, urmat de o echipă obstetricală experimentată, iar operația cezariană intenționat amânată este folositoare; fătul B este cu greutate mai mare la naștere (1820 g vs. 1550 g) și la externare (2975 g vs. 2250 g) comparativ cu fratele și cu o durată redusă de spitalizare la NICU/neonatalogie în prima perioadă postnatală; nu a existat nici o complicație maternă. **Cuvinte-cheie:** naștere întârziată intenționat, sarcină gemelară dizigotică, naștere prematură, prognostic

## Introduction

The incidence of twin pregnancies has increased in the last 10 years, and the delivery of the fetuses, especially of the second one, is a great challenge, regarding actual opportunities of intrapartum fetal monitoring, and advantages/disadvantages of planned caesarean section, in the presence of prematurity<sup>(1)</sup>. The costs of antenatal and postnatal care (for the antenatal 27 weeks and postnatal 30 days) are very high for both mother and fetuses, from the first neonatal day, being appreciated to be 20 fold higher than for a single fetus pregnancy<sup>(2)</sup>.

The high risks for perinatal mortality and morbidity induced by prematurity, and intraoperative maternal, and fetal complications had induced a special care for the decision of birth in dizygotic twin (biamniotic - bichorionic/fraternal), which is established by gestational age, uterine cervix qualities, membrane, presentations, and fetal status. Planned caesarean section for breech presentation, and electronic fetal heart monitoring were not followed by the expected/wanted results, and have shown an unexpected discordance between short-term perinatal morbidity and long-term neurological outcome<sup>(3)</sup>, the rate of cerebral palsy being increased in comparison to single fetus pregnancies<sup>(4)</sup>, and the trend (though not statistically significant) was in the opposite direction.

The intentional delayed delivery of the second twin in dizygotic pregnancy is rarely reported, and this paper is focusing on such a case, which is discussed in relation to the main issues of twinning.

## Case presentation

MG, 41-years-old, from the Romanian town of Pitești, worker, married, with a medium education, with one spontaneous birth (2800 g, healthy), two abortions, with LMP in May 15, 2014, was monitored precocious for pregnancy, and diagnosed at 16 weeks with dizygotic twins, treated with folic acid, vitamins, progesterone 200 mg/day. The patient is admitted in "Dr. I. Cantacuzino" Clinic of Obstetrics in 2.11.2014 for uterine contractions, and suspicion of rupture of membranes, being diagnosed with: IVG II P 24 weeks + 3 days dizygotic pregnancy, alive both fetuses, breech presentation fetus A, cranial presentation fetus B, intact membranes at ultrasound assessment, and ultrasound estimated fetal weights (EFW) of 690 g (A), and 700 g (B).

### Case evolution

It is initiated the treatment with corticosteroids, progesterone 200 mg/day, tocolysis (nifedipine 30 mg x 2/day), magnesium sulphate, 5% dextrose 1000 ml/day, and antibiotics.

In 17.11.2014 it is recorded the spontaneous rupture of membranes of the leading twin, and it was decided the vaginal delivery of fetus A, because we appreciated a Friedman curve delivery in normal parameters, good ripening of uterine orifice, under continuous electronic fetal heart monitoring, mother being informed about the benefits and risks.

After a short trial of labor, and a labor of 4 hours, on intravenous perfusion with 5% dextrose, vitamins, magnesium sulphate, in breech presentation with Bracht maneuver, it is delivered a girl of 920 g, Apgar score =5/6, and pH

=7.00 in the umbilical cord. The umbilical cord is sectioned, introduced in the vagina, and the mother is very carefully monitored clinically, hematologically, and bacteriologically (WBC, CRP), under treatment with antibiotics, progesterone, tocolytics, intravenous perfusions. The remaining twin is monitored twice a day with NST and once a week with ultrasound scan. Maternal, and remaining twin evolutions are normal, the placental masses are not separated. It is decided caesarean section (CS) at 33 weeks + 4 days (chronological and sonographical) for the risks of blood redistribution to fetus A placenta, and an umbilical cord procubitus loop of the remaining fetus, with high position of the head, and chorioamniotic infection (increasing WBC, CRP).

It is delivered the twin B, female 1870 g, Apgar score =8, pH =7.15 of umbilical cord blood, and a 200 g corporeal inserted placenta of fetus A, with calcium impregnations, reduced consistency, and a 450 g fundus and posterior placenta of fetus B, calcium impregnations of membranes. Uterine retraction is normal, and maternal intra- and postoperative evolution is normal, the mother being maintained in hospital for another 23 days, for her preterm babies. Baby A was admitted at NICU with moderate hypoxia at birth, repeated apnea crisis, without functional respiratory syndrome, pluri-factorial anemia corrected with blood derivatives, 70 days of gastric-tube nutrition, fourth generation cephalosporines (positive procalcitonin test), stade I retinopathy, bilateral hip risk. At the date of CS, baby A had 1550 g, and at discharge she had 2250 g. Baby B had favourable evolution, 2975 g at discharge, being breastfed plus milk formula.

## Discussion

The twinning rates across the world, and especially for the developing world, have changed, and in India, USA, and Europe it is an intermediate rate of 9-16 pairs /1000 births among the very high 18-30 pairs/1000 births (Central Africa) and the lowest of 6-9 pairs/1000 births (Latin America, South Asia, and South-East Asia) as it is provided in the most complete and comparable overview of twinning rates across the 76 low- and middle-income countries, as Romania<sup>(5)</sup>. In USA, the rate had increased from 18.9 in 1989 to 33.3 per 1000 births in 2009<sup>(6)</sup>.

Eighty years ago, Greulich WW<sup>(7)</sup>, cited by Hochstra C et al.<sup>(8)</sup>, discussed the factors involved in variable incidence of dizygotic pregnancy: times, geographic areas, seasons<sup>(9)</sup>, populations, familial, and genetics: X fragile syndrome determined by the deficiency of FMR1 protein located on chromosome Xp27.3, followed by ovarian insufficiency and premature menopause<sup>(8)</sup>, and the GDF9 and BMP15 mutations<sup>(11,12)</sup>. Dizygotic (fraternal) pregnancies were 70% from natural twins in USA<sup>(13)</sup>, but the incidence is more variable in time in comparison to monozygotic pregnancy, with a constant incidence, and this situation is connected to familial history of fraternal twins - from genetic risk of hyperovulation, diet with high content of growth factors as insulin-like growth factor, from high intake of cattle meat<sup>(14)</sup>, and mothers' advanced age because of pregnancy postponing, and necessity of medication/technologies for ovulation induction<sup>(14,15)</sup>. The Romanian patient reported pregnancy was naturally conceived, with no family history

of twins, with no preconceptional folic acid administration, as it was considered to be an explanation of twinning<sup>(16,17)</sup>.

Recently, it is not known why elder women have a higher natural rate of dizygotic twins, one explanation being the higher FSH level, which makes ovaries to be more responsive<sup>(18,19)</sup>.

The presentations in the studied case are breech/cephalic, and the literature reports in the dizygotic twins are cephalic/cephalic (40%), cephalic/non-cephalic (35%), and 25% with the leading fetus in non-cephalic (vertex) presentation, like the Romanian one<sup>(20,21)</sup>. The assigned risk associated to fetal presentations is increasing in discordance to frequencies of fetal presentations, as it is reported in "The Netherlands Perinatal Registry" for cases with a gestational age (GA) of 32+0 - 41+0 weeks<sup>(22)</sup>: cephalic-non-cephalic - OR 2.27; non-cephalic- cephalic - OR 13.63; non-cephalic - non-cephalic: OR 21.92. It was described that after the delivery of the leading fetus the presentation of the second can be changed (20% of cases<sup>(23)</sup>), to breech, converted to transverse lie, or it can be registered a cord prolapse

The most frequent dizygotic twins' gender is male/female (50%), then female/female (sororal), and male/male.

The dizygotic twins have a lower risk in comparison to monozygotic twins, but the risks of twin-infants, and of their mothers are still very high in contemporary societies. It has long been known that perinatal morbidity and mortality are in conjunction to prematurity, alone or associated to intrauterine fetal growth restriction in comparison to singletons of the same GA and/or same birthweight<sup>(24,25)</sup>, and in conjunction to the quality of hospital/maternity, qualification of medical staff, and to the timing, and route of birth. Cochrane Database Systematic Reviews<sup>(26)</sup> and Hofimeyr GJ et al.<sup>(3)</sup> revealed that the absolute rates of perinatal mortality and morbidity vary by population, country, and the moment of parturition complication (antepartum/intrapartum/postpartum). Another discussion is in relation to the higher risk of the second twin, independent to presentation, chorionicity or fetal sex<sup>(27)</sup>.

In this case, the optimal delivery timing discussed to be at 37 to 38 weeks of gestation<sup>(28-30)</sup> or near term<sup>(26)</sup>, or according to the French College of Obstetricians-Gynecologists<sup>(31)</sup> from 38 to 40 weeks, was not possible to be achieved, because maternal incompetent internal os of the uterine cervix (as we suppose to be in the Romanian case), and/or of low efficacy of tocolysis (nifedipine), and due to the premature rupture of membranes associated to the first two, as it is appreciated by literature to be the most frequent reasons for delivery before 32 weeks of gestation<sup>(32)</sup>. In the Cochrane Database Systematic Review, 2014<sup>(33)</sup>, it is compared the optimal elective delivery timing for twins from 37 weeks in uncomplicated dizygotic twin pregnancies versus an expectant management, and it was concluded that early birth at 37 weeks of gestation does not appear to be associated with an increased risk of harms, and the authors considered that there are not sufficient clinical equipoise to allow for the randomization of women to a later gestational age at birth.

When complications regarding the babies are depicted or suspected, it is proved by the last Cochrane Database

Systematic Review (November 2015) that a planned early delivery with less than 10 days to full term versus expectant management is improving primary maternal outcomes, and primary neonatal outcomes (perinatal mortality and morbidity, and neurodevelopment/ disability/ impairment at two years of age<sup>(34)</sup>). It was considered that planned caesarean section may reduce with 75% the risk of perinatal death in term twins, especially for the twin B, versus a vaginal delivery<sup>(35-38)</sup>, mainly by reducing the risk of death of the second twin due to intrapartum anoxia<sup>(39)</sup> or versus a trial of labour.

At term when the leading fetus is in breech presentation, the caesarean section was the rule at the beginning of this century<sup>(40,41)</sup>, but during time, there had been some controversies, which are discussed by some of the same authors of the previous paper<sup>(42,43)</sup>, regarding fetal morbidity and mortality. For babies under 1500 g, there was no difference in mortality and morbidity based on a 5-minute Apgar Score under 5, in multigravidas, after vaginal route vs. caesarean section, as it is revealed by the largest multi-centre study in terms of numbers by Blickstein I et al.<sup>(44)</sup>, but when the second twin is in breech presentation the cord pH is lower than for the second twin in cephalic presentation after the vaginal delivery, and more cases are admitted to NICU. According to authors, multiparity and elective caesarean seemed to have little influence on outcome measures, extremely preterm twins may have a higher risk of neonatal mortality<sup>(44,45)</sup>.

The Romanian obstetricians involved in the reported case considered that vaginal route for the leading fetus in breech presentation is safe, and the trial of labour was positive, in the favorable conditions of the case, on continuous electronic monitoring. After a retrospective study of 10 years<sup>(46)</sup>, it was concluded that the attempting vaginal route versus planned caesarean delivery for the first twin in dizygotic pregnancy is possible based on correct, and attentively intrapartum criteria, after a precise protocol, which must be followed by a experienced obstetrician comfortable in the performance of vaginal breech delivery, and well trained, skilled midwives, in the presence of an anesthesiologist, with the existence of an adequate operative room for an emergency caesarean section. All these criteria were present in the Romanian case.

The choice of CS for the second twin after the vaginal delivery of the leading twins is more frequent in term fetuses than in preterm pregnancies<sup>(47)</sup>, the indications are maternal reasons, or complications of labor/delivery, or second twin in a non-cephalic presentation (breech presentation, or malpresentations) which sometimes are emergency indications<sup>(48,49)</sup>. Most recent retrospective studies<sup>(50,51)</sup>, and a population based study from Denmark<sup>(52)</sup> state that there is no advantage in elective C-section over vaginal delivery in the case of twin births in which the first twin is in cephalic presentation and the second is not in cephalic presentation; and even an increase of two-fold<sup>(48)</sup> or four-fold<sup>(52)</sup> for the second twin risk delivered by CS after the vaginal route of the leading twin. In the Danish study<sup>(52)</sup> the Apgar Score less than 8, and pH umbilical cord under 7.1 were significantly higher compared to the vaginal delivery route of the second twin in non-cephalic position (OR 6.2; 95% CI 2.1-18).

The interval between the deliveries of the twins is a very much discussed and analyzed issue. After the delivery of the fetus A, it appears an interval free of uterine contractions of 15-30 minutes, which can be longer than 60 minutes, during which uterine bleeding and the remaining fetus must be very well assessed. Studies on the influence of the birth interval on neonatal morbidity have contradictory results.

In the literature of the last 10 years, there are considered different intervals between the two deliveries: 15 minutes in France<sup>(53)</sup>, 30 minutes in USA<sup>(54)</sup>, and in Germany<sup>(55)</sup> the second twin delivery was recorded at different intervals (15 minutes: 75.8%; 16-30 minutes: 16.4%; 31-45 minutes: 4.3%; 46-60 minutes: 1.7%; >60 minutes: 1.8%; 72 instances).

In the "Twin Birth Study", held for 15 years, from the German Region Hesse, the birth interval between twins was on average  $3.6 \pm 1.5$  minutes in the group with planned caesarean sections, and with longer duration (56.2%) in the group with planned vaginal delivery (of  $10 \pm 16.7$  minutes), and the conclusions were that no significance of the birth interval on child morbidity can be drawn from the "Twin Birth Study", and that the obstetrician who monitors the pregnancy/labor/birth may accelerate or not the procedures/maneuvers for the second twin delivery<sup>(56)</sup>.

There is a historical recommendation that the delivery of the second twin must not be later than 60 minutes<sup>(57)</sup>, but the German obstetrician was citing cases with a delayed delivery of the second twin from 35 to 169 days, and actually in different countries the possibility of increasing the interval between the births of dizygotic twins is much discussed: The Netherlands<sup>(58)</sup>, Spain<sup>(59)</sup>, Italy<sup>(60)</sup>, with

analysis of maternal and infants outcome (short and long time follow-up), some of the offspring being considered miscarriages (the Spanish cases). In Romania (2005), it was presented by BBC a case with an interval of 59 days between the deliveries of fraternal.

### Initial Neonatal Outcomes

Neonatal outcome is dominated by prematurity, low Apgar Score and low pH of blood cord, duration of admission in NICU especially for respiratory distress syndrome, neonatal seizures<sup>(61)</sup>, which is more severe for the second twin, and is associated to birth trauma - cervical and brachial plexus, facial nerve, fractures of skull, and clavicles, soft tissue lacerations<sup>(62)</sup>. There are to be added the intrinsic abnormalities connected to twins genetics, especially for male fetuses from mothers with X fragile syndrome/GDF9 and BMP15 mutations, which are prone for mental retardation or neurodegenerative disorders in adult life<sup>(8,10)</sup>.

The short-term neonatal outcomes of the twins are listed in Table 1.

The Romanian obstetricians involved in the management of the reported case are wondering about the explanations/determinants/factors which may explain the evolution. One explanation is represented by the recommended drugs (progesterone, tocolytics, antibiotics), but we consider the placentae of the twins to be more important. The placenta of the leading fetus did not separate after the first birth, and the placenta of the fetus B permitted a future normal evolution. The placenta of fetus B was 450 g, larger than that of fetus A, of 200 g, with calcium stores. This hypothesis is discussed by the

**Table 1** Short term neonatal outcomes of twins

	<b>EFW (g)</b> at maternal hospital admission	<b>Birth GA (weeks)</b> + weight (g)	<b>Apgar Score</b> 5-10 minutes	<b>Hospital Admission Duration</b> (days)	<b>pH blood cord</b> at admission + duration in NICU (days)	<b>Initial Neonatal Morbidity</b>
<b>Fetus A</b>	690	26 920 (1550 at CS for fetus B)	5/6	78	7 50	Moderate hypoxia at birth Anemia Retinopathy stage I Hip risk
<b>Fetus B</b>	700	34 1870	8	31	7.25 2	Umbilical hernia
<b>Babies' weight at discharge (g)</b>						
<b>Fetus A</b>				<b>Fetus B</b>		
<b>2250</b>				<b>2975</b>		

Legend: EFW; estimated fetal weight; GA: gestational age



most recent Cochrane Database Systematic Review<sup>(63)</sup>, with the conclusion that the biochemical tests (estrogens, human placental lactogen) for placental functions are not sufficient markers, or are of low or very low evidence.

## Conclusions

Planned vaginal delivery at a multipara can be assumed in breech presentation, in a case with cervical incom-

petence, short labor, and a fetus below 1000 g, after a precise protocol, followed by experienced obstetrical/neonatalogical teams. An intentional delayed CS delivery is feasible with very few risks. Fetus B is larger at delivery than fetus A at the moment of CS (1870 g vs. 1550 g), and at discharge (2250 g vs. 2975 g), and fetus B has a very short admission in NICU/preterm wards in comparison to leading fetus. No maternal complication appeared. ■

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