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## Complications of twin pregnancies

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### ABSTRACT

Twin pregnancy in the population of Europe is relatively common. One in eighty deliveries results in at least two newborns' coming to the world. Parents expecting twins are usually excited about the vision of large family, however for an obstetrician a multiple pregnancy is a challenge that involves more complications than singleton pregnancy. The risk of complications exceeds 50%, therefore twin pregnancies are considered as high risk. The most common complication is premature birth, which may result in respiratory failure of the newborn, necrotizing enterocolitis or intracranial hemorrhage. Other complications, that are characteristic for twin pregnancies only, are intrauterine growth restriction, intrauterine fetal death one of the fetuses, hemodynamic disorders due to the connecting blood vessels within the placenta in a monochorionic pregnancy or umbilical cord collision in a monoamniotic pregnancy. Perinatal care in a multiple pregnancy should include a determination of chorionicity and amionicity, prevention of premature labor and rapid diagnosis and treatment of complications. Over 75% of twin pregnancies are delivered via caesarian section which is also burdened with sequelae. Likewise, women pregnant with more than one fetuses suffer from anemia, hypertension, hyperemesis gravidarum and intrahepatic cholestasis of pregnancy more often than those in singleton pregnancies. Despite frequent complications, thanks to intensive perinatal care (numerous gynecological and ultrasound examinations, in some cases the necessity of hospitalization), perinatal mortality decreases and more twins develop properly each year.

**Keywords:** Twins, multiple pregnancies, perinatology, monochromic pregnancy, monoamniotic pregnancy, twin-to-twin transfusion syndrome, umbilical cord collision, premature labor

## **1. INTRODUCTION**

The frequency of twin deliveries in Europe is now 1 in 80 live births [1]. In the USA rate for twins is 1 in 83. Throughout the years multiple pregnancy has become more frequent due to various reasons [2, 3]. One of them is delayed childbearing. In the year 2002, 18.9% of twins were delivered by mothers between the ages of 45 and 49 years [4]. Another important factor which increases the risk of a multiple pregnancy is the use of reproductive technologies e.g. fertility medications and in vitro fertilization [5]. Others include impregnation during lactation or three months after abandonment of contraceptive pills. Family history of multiple pregnancies or mother's overweight can also influence the chance of twin pregnancy.

Multiple births present numerous medical risks to the pregnant woman and fetuses. The most common complications are premature birth, low birth weight, congenital defects, intrauterine fetal death. Another possible outcome is complication characteristic for monochromic pregnancy e.g. twin-to-twin transfusion syndrome, twin reversed arterial perfusion syndrome or characteristic for monoamniotic pregnancy like umbilical cord collision. Women pregnant with twins suffer from pregnancy-induced hypertension, toxemia, anemia, hyperemesis gravidarum, vaginal-uterine hemorrhage more often [6,7].

## **2. COMPLICATIONS MUTUAL TO SINGLETON PREGNANCY**

Multiple pregnancy might be complicated by the same medical conditions as singleton pregnancy, however its incidence is much higher. The most common is premature birth and congenital malformations.

### **2. 1. Premature birth**

Preterm birth is main reason (30%) of neonatal death with a total of one million deaths annually [8]. Among twin gestations the rate of late-preterm birth (34-37 week of gestation) reaches 50% [9, 10]. Furthermore, one third of neonates born at 34–35 weeks of gestation pertains to twins [11]. Perinatal infection may have a more serious outcomes for fetus in preterm twin births than singleton pregnancy. Infants born prematurely are at greater risk of mortality and morbidity than infants born at term. Complications include acute respiratory, central nervous system, gastrointestinal, immunologic, hearing, and sight problems. Long-term dysfunctions are motor, cognitive, behavioral, social-emotional and growth problems [12]. Corticosteroids therapy before labor decreases respiratory distress syndrome, necrotizing enterocolitis, systemic infections and perinatal mortality [13]. Due to complications of vaginal delivery in preterm twin pregnancies, cesarean delivery is regarded to be safer, particularly for second twins due to incidences of hypoxia after delivery maneuvers, cord prolapse or premature placental separation [14].

### **2. 2. Congenital defects**

The risk of a congenital defect in a multiple pregnancy is around 70% higher than in a singleton pregnancy [15]. Congenital anomalies may be the consequence of the teratogenic insult that induces the twinning [16]. Another theory lead the subfertility (and the factors associated such as advanced maternal age, obesity and fertility treatments) as an etiology of

twinning, which are also considered as risk factors of birth defects. Alternative mechanisms include twinning itself e.g. crowding, insufficiency of nutrition supply, and for monozygotic twins, vascular anastomosis [17]. In multiple studies have been recorded increased risk for a number of congenital defects among twins, including anencephaly, hydrocephalus, coarctation of the aorta, tetralogy of Fallot, pulmonary valve stenosis, oesophageal atresia with or without tracheoesophageal fistula, cleft lip with or without cleft palate, anorectal atresia and hypospadias [17-21].

### **3. COMPLICATIONS CHARACTERISTIC FOR MULTIPLE PREGNANCY**

Complications characteristic for multiple pregnancies include selective intrauterine growth restriction or intrauterine fetal death of one of the fetuses, hemodynamic disorders due to the connecting blood vessels within the placenta in a monochorionic pregnancy (e.g. twin-to-twin transfusion syndrome and twin reversed arterial perfusion syndrome) or umbilical cord collision in a monoamniotic pregnancy.

#### **3. 1. Selective intrauterine growth restriction**

Selective intrauterine growth restriction (sIUGR) occurs at a similar rate (11-12%) in both monochorionic and dichorionic pregnancies [22]. Selective IUGR in twin pregnancy might be measured in percentage disparity between fetuses in estimated fetal weight (EFW), actual birth weight, abdominal circumference, estimated fetal weight or actual birth weight of one twin falling below the 10th centile [23]. Selective IUGR in dichorionic pregnancies is caused by placental insufficiency (like in singleton pregnancies). Abnormalities in Dopplers of umbilical artery or ductus venosus foreshadow poor outcomes [24]. Treatment of dichorionic pregnancies affected by sIUGR is complicated when the IUGR twin is at risk at an early gestation. Iatrogenic preterm delivery before 28 weeks of gestation expose one of the twin to serious sequelae of prematurity, whereas expectant management may lead to intrauterine fetal demise of the IUGR twin and in consequences preterm delivery of the second twin.

The risk of neurological injury or demise in the surviving twin is fairly low. The risk of preterm delivery after intrauterine fetal death of one twin is about 54%, demise of other twin about 3% and neurodevelopmental damage in surviving twin is reach 2% [25]. In over 95% of monochorionic pregnancies are present vascular anastomoses that allow exchange of blood between the circulations of twins [26]. sIUGR in monochorionic pregnancies is caused by unequal placental division, but the complications are determined by the type of vascular anastomoses. Umbilical artery Doppler allows classify disorders and set apart low-risk and high-risk subgroups. After 26–28 weeks, the complications of preterm delivery are less probable than the risks of fetal intervention. Nonetheless, sIUGR pregnancies identified before the third trimester and with high risk of perinatal complications are considered for fetal intervention. Invasive treatment methods contain laser coagulation of the vascular anastomoses between the fetal circulations, selective reduction or termination of the whole pregnancy [27].

#### **3. 2. Single intrauterine fetal demise**

Single intrauterine fetal demise (sIUFD) pertains to approximately 3.7 – 6.8 % of twin pregnancies [28, 29]. Death may occur any trimester and increases mortality and morbidity of

the survivor twin. Complications include preterm labour or even the death of the co-twin. The etiology of sIUFD in twin pregnancy could be both similar to that in singletons or characteristic to the twin pregnancy. The reasons of sIUFD might be genetic and anatomical anomalies, placental insufficiency, placental anastomoses, abruption, absolute or relative growth restriction, cord defects, infections, and maternal complications such as diabetes and hypertension [30].

50-70 % cases of sIUFD pertain to monochorionic twinning [31]. Poor outcomes of the surviving co-twin is a common complication. The risk of co-twin death after 14 weeks' gestation in monochorionic pregnancy is 12 %, whereas in dichorionic pregnancy is about 4%. After 20 weeks of gestation monochorionic co-twins are six times more likely to de cease than dichorionic co-twins. The risk of neurological disorders in the surviving twin appear to 18 % for dichorionic pregnancy and 1 % for monochorionic pregnancy [32, 33]. Differences in survival rate to the disadvantage of monochorionic twins are caused by vascular anastomoses between circulations of fetuses, which are frequently present in that kind of placentas and almost never seen in dichorionic ones. In monoamniotic pregnancies, cord entanglement is potential risk factor of the intrauterine death of one twin.

Medical procedures in sIUFD should be preceded by defining gestational age and chorionicity. Dichorionic pregnancies complicated by sIUFD are at greater risk of preterm delivery before 34 week and reaches to 57 %. In case of absence of spontaneous preterm delivery or other perinatal complications, iatrogenic preterm delivery is not recommended. Dichorionic pregnancies without other obstetrical problems can be delivered at term, while monochorionic pregnancies are more complicated to manage and are often terminated between 34 and 37 weeks [30].

### **3. 3. Twin-to-Twin Transfusion Syndrome**

Twin-to-Twin Transfusion Syndrome (TTTS) pertain to 10-15% of all monochorionic pregnancies. Most of the monochorionic twins have arteriovenous anastomoses in blood circulation, but also appears arterio-arterial and veno-venous. Commonly, this transfusion is equal, however in twin-to-twin transfusion syndrome the blood flow can become unbalanced. One of the twins, called "Donor Twin" have impaired circulation due to transmission part of his blood via anastomoses to second twin, called "Recipient Twin". The results are chronic hypovolemia, oliguria, and oligohydramnios in the donor, and polycythemia, hypervolemia, polyuria and polyhydramnios in the recipient [34, 35].

The diagnosis is performed by prenatal ultrasound scan. Quintero's criteria distinguish five stage with increasing severity. The polyhydramnios–oligohydramnios (stage I) state is associated with a diminished bladder in the donor (stage II), signs of cardiovascular overload and Doppler anomalies in recipient twin (stage III), hydrops fetalis (stage IV) and intrauterine fetal death one or both twins (stage V) [36]. In cases diagnosed before 20 weeks of gestation, untreated, mortality is close to 100%.

Previously the most common method of treatment was amnioreduction [37, 38]. In the 1990s it was announced an endoscopic technique of laser ablation of anastomoses. After some modifications, laser ablations have taken the lead in treatment severe TTTS ( $\geq$  stage II). In multicenter randomized control trial, which compares endoscopic laser surgery and serial amnioreduction for severe twin-to-twin transfusion syndrome, it was revealed that higher survival rate has twins that underwent laser ablation of anastomoses than amnioreduction (76% vs. 56%). The incidence of brain disorders (define by the presence of periventricular

leukomalacia on imaging) was also lower in group with ablation of anastomoses. Likewise, twins after in utero laser ablation were delivered 4 weeks later than those after amnioreduction (33 vs 29 weeks) [39].

### **3. 4. Twin reversed arterial perfusion syndrome**

Twin-reversed arterial perfusion syndrome (TRAP) occurs in 1% of monochorionic pregnancies. The incidence of TRAP is estimated to be 1 in 35,000 pregnancies [40]. TRAP is extended version of a twin-to-twin-transfusion-syndrome and is also associated with arterial and venous anastomoses between twins. Blood-transfer from donor fetus to the impaired twin caused reversion of circulation in receiving twin, passive perfusion, decreased oxygen saturation, underdevelopment and eventually atrophy of the heart. The receiving twin becomes a parasite-like organism dependent on the blood supply from the donor twin. Deoxygenated blood from the healthy donor-twin runs to acardiac twin via the umbilical cord. This poorly oxygenated blood is sufficient to supply near-by located structures like the lower limbs or the intestines. Whereas the blood circulation in distant parts like head or upper extremities is deficient, which lead to underdevelopment of this structures [41].

The diagnosis of TRAP during ultrasound is realisable during the first trimester. An acardiac twin may be detected sonographically by underdeveloped upper and lower extremities, without an evidence of heart beating. Doppler demonstrates reversed arterial perfusion from the donor twin towards the acardiac twin. Most frequently blood supply enters the parasite-like twin via a single umbilical artery. Blood-flow in veins also indicates reversed perfusion [42].

The prognosis in TRAP syndromes is lethal for acardiac twin. Due to high output cardiac failure, the fetal mortality of the donor twin is fairly high [50-75%]. Usually, the delivery is performer as a caesarian section around 32 week of gestations due to preterm labor or rupture of membranes as a consequences of polyhydramnios. Long-term outcome of the surviving fetus is determined by the presence of cardiac insufficiency and the consequences of premature birth [41].

Treatments of TRAP has many possible strategies and depends on the condition of the donor twin. Prevention of premature birth includes amniotic drainages, tocolysis and digitalis-treatment to support the cardiovascular system of the pump twin. First attempts consist in elective hysterotomy. Acardiac twin was removed, while the pumping twin was leaving in utero [43]. These interventions have been replaced by less invasive operative procedures to close blood-flow between fetuses: fetoscopic selective ligation of the acardiac cord, fetoscopic embolization or alcohol ablation of the umbilical vessels or ablation with other thrombogenic material (e.g. platinum coils). Newer strategy is laser-photocoagulation of the arterio-arterial and veno-venous anastomoses. Indication for obstruction-inducing treatments includes: polyhydramnios with a vertical pocket above 8 cm, abdominal circumference of the acardiac twin larger or equal to the donor twin, abnormal Doppler-flow-patterns or hydrops of the pumping twin and monoamniotic twins [44].

### **3. 5. Umbilical cord entanglement**

Monoamniotic pregnancy is very rare. It pertains to 1% of all monozygotic twins, which gives 0.004% of all live births. The perinatal mortality rate fluctuates between 28–60%. These pregnancy may have unique medical conditions like conjoined twins, high prevalence of structural disorders or cord entanglement [45]. Umbilical cord entanglement is specific for

monochorionic and monoamniotic twinning, although rare cases of cord collision in spontaneous and iatrogenous septostomy in diamniotic twins have been described. Ultrasound from 10 gestational weeks may diagnosed umbilical cord entanglement. Sonographic criteria are: single placenta, lack of separating membrane and same sex. In case of confirmation the diagnosis it is recommended to perform regular ultrasound follow-up with color Doppler imaging. Nevertheless, this increased diagnosis do not improved significantly survivability, management and outcome of fetuses [46].

High perinatal mortality is a result of prematurity, cord complications and associated congenital disorders. The mode of birth and age of gestation while delivery are still under discussion. In order to avoid intrauterine complications in late pregnancy and minimize poor outcomes of prematurity, cesarean section at 32 week of gestation is recommended. Abdominal delivery is advised to avoid intrapartum accidents of collision. Absence of optimal protocol causes the management of monoamniotic twins is inconvenient. Ultrasonographic investigation and documentation of the umbilical cord entanglement are recommended in making decision about delivery [47].

#### **4. MATERNAL COMPLICATIONS IN TWIN PREGNANCY**

Woman in multiple pregnancy are at greater risk of anemia, hypertension, postpartum hemorrhage, urinary tract infections, puerperal endometriosis, caesarian section, hyperemesis gravidarum and intrahepatic cholestasis of pregnancy. The incidences of premature rupture of membranes, gestational diabetes mellitus, bleeding in third trimester are similar for singleton and twin pregnancy [48]. Hypertensive disorders of pregnancy are at the forefront of the complications of twin gestation and 14% women expecting twins suffer from this disease. Hypertensive disorders are the reason of 15-20% deaths of pregnant women, which makes it second cause of maternal death in the United States (the first one is thromboembolism]. On that account, the risk of pulmonary embolism and stroke may increase even 3 to 12 times during third trimester and periparturient. Likewise, hypertension leading to iatrogenic premature delivery is associated with high perinatal mortality and morbidity [49].

Intrahepatic cholestasis of pregnancy is a liver disease, which manifest by maternal pruritus and increased serum bile acids. This medical condition is fraught with high risk of poor outcomes for fetuses e.g. spontaneous and iatrogenic premature delivery, meconium staining of the amniotic fluid and stillbirth. Twin pregnancy is associated with an increased risk of intrahepatic cholestasis of pregnancy which may lead to 6,7% whereas in singleton incidence rate is about 1,3% [50].

#### **5. CONCLUSIONS**

Studies from all over the world suggest that twin pregnancies are at greater risk of maternal, fetal and neonatal complications. There are many factors that have influence on postpartum outcomes e. g. preterm birth, chorionicity, amniocity, mode of birth and comorbidities. In spite of numerous difficulties, with assistance of intensive perinatal care (multiplicities gynecological and ultrasound examinations, maternal hospitalization), perinatal mortality and morbidity decreases and twins develop properly after the delivery.

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