Twin pregnancy – physiology, complications and the mode of delivery

ANNA DERA¹, GRZEGÓRZ H. BRĘBOROWICZ¹, LOUIS KEITH²

Abstract
The aim of the article is to present actual knowledge concerning twin pregnancy. After the physiological changes observed during such pregnancy, main complications such as intrauterine growth restriction (IUGR), prematurity, premature rupture of membranes (PROM) and hypertension are discussed. The paper ends with discussion about the possible routes of delivery in twin pregnancy.

Key words: twin pregnancy, IUGR, hypertension, prematurity, mode of delivery

The incidence of multiple births has been rising steadily for over past 30 years. The reasons for this trend include advances in reproductive medicine as well as a greater proportion of older pregnant mothers who naturally have a higher incidence of multiple gestations. Twin pregnancies in an unmedical population comprise 1% of all pregnancies, but account for at least 10% of prenatal mortality [1, 2]. The individual twin’s risk of prenatal death is at least three times that of a singleton, and the incidence of stillbirth is twice that of singletons [3, 4]. Low birth weight and prematurity are the main causes of high prenatal morbidity and mortality in twins, whereas malpresentation and the hazards of delivery are next in order of concern. For these reasons, twin pregnancy is considered a high-risk pregnancy; different aspects of the risk include the mode of delivery, which remains a subject of a controversy and discussion among obstetricians.

Multiple pregnancies
Multiple gestation is a pregnancy where more than one fetus develops simultaneously in the womb. Depending on the number of developing fetuses, one can distinguish twin, triplet, quadruplet, or quintuplet pregnancy, and so forth. The mechanism of development of multiple pregnancies is one of the most interesting in the etiology of the human development. Twins pregnancies occur naturally about one in every 90 births and result from 1 of 2 mechanisms that determine zygosity [5].

Dizygotic twins
Approximately two-thirds of twins in a Caucasian population are dizygotic or fraternal, their incidence of 7-11/1000 births increasing with increasing maternal age [6]. They result from simultaneous ovulation of two oocytes and fertilization by two different spermatozoa. Both zygotes have very different genetic constitutions, and each implants individually in the uterus and develops its own placenta, its own amnion and its own chorionic sac. Conditions, which can influence the development of dizygotic twin pregnancy, include maternal race, age and weight, past obstetric history, genetic predisposition and the time of the year during which the conception took place. Most if not all are associated with an increase in the level of gonadotropin hormones in the maternal blood serum.

Monozygotic twins
The second type of twins develops from a single ovum and is known as monozygotic or identical twins. This phenomenon is a random genetic event, which occurs 1 in 250 pregnancies. Depending on the splitting of the primary zygote at various stages of development into two genetically identical embryonic structures, three types of monozygotic twin pregnancies are distinguished: dichorionic diamniotic – if the splitting occurs before 4 days after insemination; monochorionic diamniotic – when the split occurs between day 4 and 7 day; and, finally, monochorionic monoamniotic – when it occurs more than 7 days after insemination. Monozygotic twinning occurs independently of ethnicity, maternal age, parity, nutritional status and environmental factors, but the rate of occurrence may be doubled after induction of ovulation and is increased with in-vitro fertilization. Monochorionic placenta increases the risk of early pregnancy loss (before 24 week) and may result in serious pregnancy complications such as twin-to-twin transfusion syndrome [7]. Monochronicity and monozygosity are associated with increased risk of preterm birth as well as an increased risk of congenital anomalies, growth restriction and prenatal death [8-10].

The incidence of twin births
The rate of multiple pregnancies has been rising significantly world wide, especially in countries such as Canada and United States. For example, the rate of multiple births in Canada increased from 1.9% in 1981 to 2.5% in 1997 [11]. The phenomenon in these countries is mainly associated with increased numbers of births to older mothers and increased use of fertility treatments as well as assisted conception. The increase in the incidence of multiple pregnancies in Poland has been rather steady and not so visible, considering the overall increase in births; it reached its peak between 1980 and 1991 and then stabilized after 1998 [12]. This steady increase is considered mainly associated with the limited availability of assisted reproductive techniques, as well as a young age of the mother and cultural and religious differences, which do not favor so-called "unnatural" forms of therapy.

It is generally recognized that 97% of multiple pregnancies are twin pregnancies [5]. Approximately 40% of these
physiologic changes in multiple pregnancy

Pregnancy is a time during which multiple adaptive changes take place in the maternal organism to allow optimal conditions for developing fetus. The physiologic adaptations occur in the mother in response to the demands of pregnancy. These demands include support of the fetus, protection of the fetus, preparation of the uterus for labor and protection of the mother from potential cardiovascular injury at delivery. All maternal systems are required to adapt; however, the quality, degree, and timing of the adaptation varies from one individual to another and from one organ system to another. Multiple pregnancy significantly affects the ability of the mother to adapt to the demands of pregnancy. The knowledge and understanding of these physiologic adaptive changes allows health care providers to foresee pathology, anticipate the effects of multiple pregnancy on underlying medical conditions and to manage pregnancy-associated complications. These physiologic changes are mainly associated with disturbances of the adaptive mechanisms. Multiple pregnancy, as a high-risk pregnancy, is associated with changes, which are a little bit different from those, which take place in a singleton pregnancy. This fact is mainly associated with the presence of more than one fetus in the uterine cavity. Of great importance, these physiological changes may become so intense that they border on pathological. The changes may be divided into anatomical and physiological.

Anatomical changes

The anatomical changes of multiple pregnancy are mainly associated with the number of fetuses in the uterine cavity and, at the same time, the size of uterus within the abdominal cavity. The size of the uterus is almost the same as singletons until the second trimester of pregnancy; after the 18 week, it is twice as big as in a singleton pregnancy and, in the 25th week, the uterine size is the same as a term singleton pregnancy. Another important anatomical change is associated with cervical length, which is crucial in terms of the duration of the gestation. During twin pregnancy, the cervical length shortens about 0.8 mm a week, a circumstance that not only acts as a risk factor but also definitely predisposes this type of pregnancy to a premature birth. Further, the amniotic fluid volume is greater than in the singleton pregnancy. This volume greatly increases until the second trimester and then stabilizes during the beginning of third trimester, decreasing between the 33rd and 36th weekly. The normative values for MAP are the same as in singleton pregnancy (525 cm). Finally, weight gain in multiple pregnancies is different than in singleton pregnancy. According to American College of Obstetricians and Gynecologists, weight gain during multiple pregnancy should be approximately 16 to 20.5 kg, which is approximately 0.68 kg/week. At least one study has indicated that weight gain below 0.39 kg/week may be associated with an increase in premature birth and its consequences [15]. Luke et al. reported that maternal weight gain early during pregnancy might improve outcome of twins as well as triplets [16-19]. This conclusion was based on the assumption that multiple pregnancies involve greater nutritional requirements than in the case with singletons. When this need is appropriately met by adequate maternal weight gain during pregnancy, improved outcomes were observed in terms of prolonging length of gestation and in larger birth weights [16, 17].

Physiological changes

Circulatory system

The changes in the circulatory system are mainly associated with the increased demand for oxygen. This appears early (5 weeks after the last menstrual period) and is much more intensified compared to singleton pregnancy. Due to increased demand for oxygen, the cardiac output increases 35-40% by the end of first trimester until it is approximately 50% greater than that of a nonpregnant woman. This phenomenon is mainly associated with the increased volume of the circulating blood – about 35% during multiple pregnancies comparing to singleton pregnancy. The etiology of this process is controversial, but is thought to be associated with an activation of rennin-angiotensin-aldosterone system and increased levels of placental hormones [20]. Maternal cardiac output increases as early as 10 weeks of gestation and peaks at 30-50% over nonpregnant values by the latter part of the second trimester. This rise (from 4.5 l/min nonpregnancy to 6.0 l/min in the second trimester of pregnancy) is sustained for the remainder of the pregnancy. The increase in cardiac output is associated with an increase in heart rate by 15-20% over the nonpregnant level by the end of the first and second trimester [21]. It is likely that the increase in heart rate is a secondary (compensatory) effect resulting from the decline in systemic vascular resistance during pregnancy. Stroke volume increases by approximately 25% to 30% by the end of second trimester and remains at this level until term. The increase in stroke volume is due primarily to an increase in cardiac preload which is due, in turn, to a disproportionate increase in circulating blood volume [22]. Left ventricular end-diastolic volume increases during gestation, whereas end-systolic volume remains unchanged resulting in an increase in ejection fraction. Blood pressure is the product of cardiac output and systemic vascular resistance and reflects the ability of the cardiovascular system to maintain perfusion to the various organ systems, including fetoplacental unit. The blood flow through the pregnant uterus increases 20 to 40 times compared to singleton pregnancy. The high concentration of progesterone in multiple pregnancy causes a decrease in systemic vascular resistance, which is associated with a decrease of the diastolic blood pressure. The greater mass of fetuses, amniotic fluid and placentas may readily compress the neighboring vessels such as the aorta and inferior vena cava causing the supine hypotensive syndrome. This syndrome is a result of

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profound drop in venous return for which the cardiovascular system cannot compensate. Physiologic compensatory mechanisms in the maternal circulation include increase in the heart rate and increase resistance in the vasculature of the lower limbs.

**Respiratory system.** There are numerous changes in the maternal respiratory system during pregnancy. These changes result initially from the endocrine changes of pregnancy and later, from the physical and mechanical changes brought about by the enlarging uterus. As the enlarging uterus enters the abdominal cavity, it compresses veins and causes increase venous pressure in the lower parts of the maternal body; this, along with the decrease in the oncotic pressure, causes the patient to experience edema around the ankles. The elevation of the relaxed diaphragm, which occurs as the enlarging uterus enters the true abdominal cavity, causes a decrease in the oncotic pressure as well as the tone of the lower esophageal sphincter. The upward displacement of the stomach due to the enlarging uterus, enters the true abdominal cavity, causes a decrease in the oncotic pressure, food absorption as well as the tone of the lower esophageal sphincter. The upward displacement of the stomach due to the increased size of the uterus secondarily displaces the intraabdominal segment of the esophagus into the thorax. This then causes a reduction in tone of the lower esophageal high-pressure zone (LEHPZ), which normally prevents the reflux of acidic gastric content at the same time causing pyrosis (heartburn) in the pregnant women.

**Renal Physiology.** During pregnancy the glomerular filtration rate (GFR), as measured by creatinine clearance, increases by approximately 50% by the end of the first trimester to a peak of around 180 ml/min [24]. This results in a decrease in serum urea nitrogen and creatinine levels during pregnancy, such that a serum creatinine value of greater than 0.8 mg/dl may be an indicator of underlying renal dysfunction. An additional effect of the increased GFR is an increase in urinary protein extraction. Indeed, urinary protein loss of up to 260 mg per day can be considered normal during pregnancy [25]. These functional changes are not significantly different between singleton and twin pregnancies.

**Hematologic System.** Circulating blood volume increases in pregnancy to maintain preload and thereby cardiac output. There is a similar but less pronounced increase in red cell mass of approximately 30% in both singleton and twin pregnancies. This increase in red cell mass lags significantly behind the change in plasma volume, which occurs later in pregnancy. The difference in timing between the increase in red cell mass and plasma volume expansion results in physiologic fall in hematocrit in the first trimester despite adequate iron stores (physiologic or dilutional anemia of pregnancy), which persists until the end of the second trimester. The number of erythrocytes increases approximately 25% in comparison to singleton pregnancy. Erythropoiesis is stimulated by erythropoetin, which increases in pregnancy under the influence of placental hormones (chorionic somatotrophin, progesterone, and possibly prolactin) and dilutional anemia [26]. This dilutional effect also leads to decrease in circulating platelet count (gestational thrombocytopenia) [27]. In contrast, circulating white blood cell counts increase in pregnancy due to a selective bone marrow granulopoiesis. This increase peaks at around 30 weeks of gestation and although a white blood cell count of 5000 to 12,000/mm³ is considered normal in pregnancy only around 20% of women will have a white blood count of greater than 10,000/mm³ in the third trimester [28].

Pregnancy is associated with changes in the coagulation and fibrinolytic cascades that favor thrombus formation. These changes include an increase in circulating levels of factors XII, X, IX, VII, VIII, von Willebrand factor and fibrinogen. Factor XI decreases, and levels of prothrombin (factor II) and factor V are unchanged. In contrast antithrombin III and protein C levels are either unchanged or increased, and protein S levels decrease in pregnancy [29]. The effect of these changes is an increased predisposition to thrombosis during pregnancy and puerperium. The hypercoagulable state of pregnancy helps to minimize blood loss at delivery. However, these same physiologic changes also put the mother at increased...
Care of the mother in twin pregnancy

The main aim of prenatal care during pregnancy is to achieve fetal maturity, to plan an optimal method of delivery, and to achieve the best possible neonatal outcome, which will guarantee normal physical and psychological development of the children. These aims are the same for singleton and multiple pregnancies. The physician should make sure that the pregnancy as well as the circumstances of delivery are as safe as possible for the mother and the fetus. Both are possible with the knowledge of the numerous complications, which may occur during multiple pregnancy (Table 1). Using early prophylactic-diagnostic methods, one can detect different pathologies, which occur more often in multiple than in singleton pregnancies. Multiple gestation is associated with higher rates of almost every potential complication of pregnancy, with the exception of postterm pregnancy and macrosomia. Antepartum complications develop in over 80% of multiple pregnancies as compared with approximately 25% of singleton gestations [30]. Some of specific complications are discussed in detail below. The knowledge of these complications allows early detection, prophylaxis and treatment of these pathologies.

Preterm Labor and Birth

Preterm (premature) labor and birth occurs in 7% to 12% of all deliveries, but accounts for over 85% of all perinatal morbidity and mortality [31-33]. Spontaneous preterm birth is a clinical diagnosis characterized by increasing intensity and frequency of uterine contractions, leading to effacement and dilation of the cervix, and culminating in expulsion of the products of conception before 37 weeks of gestation. Approximately 57% of twin pregnancies deliver before 37 weeks of gestation although not all preterm deliveries are spontaneous.

Several tests have been introduced to identify women at high risk of preterm labor and birth. Cardiotocography as well as home uterine activity monitoring allows early uterine activity monitoring at the same time early detection of preterm labor as well as medical intervention to stop the uterine contractions (tocolysis). Serial sonographic measurement of cervical length, which can identify some twin pregnancies at risk for preterm birth. Cervical length measurement has low positive predictive value but is reassuring in symptomatic women. One study demonstrated that women in twin pregnancy and preterm contractions with cervical length ≤ 2.5 mm have a increased risk of delivering within 7 days [34].

Fetal fibronectin (fFN) in cervicovaginal secretions measured at 22 to 34 weeks of gestation is useful as a marker for preterm birth in singleton pregnancies and may be of some predictive value in twin gestations. It is indicated that 99% of patients with a negative fFN test will not deliver within 7 days.

It is well indicated that obstetric health providers are getting better at identifying women at risk of preterm birth but their ability to prevent this adverse outcome is limited. A number of interventions have been recommended in attempt to prevent preterm birth:

- Bedrest and hydration are thought to be a factor, which supports the reduction of uterine activity. However, numerous studies have failed to show that bed rest decreases the risk of preterm birth, lengthens gestation and improves neonatal outcome in multiple gestations.
- Tocolytic therapy – the aim is to increase the gestational length of multiple gestation by decreasing of the uterine muscle reactivity or uterine contractions. This type of pharmacotherapy is associated with a controversy among different authors. According to Roelts-Paletnik and Morrison, it is very important to correctly qualify the patient for this therapy in order to accomplish the expected result. This therapy should be aimed for women with diagnosed preterm labor with the use of objective methods such as cervical length or fetal fibronectin [35]. Different view is represented by Oyelese and associates, who distinguish prophylactic, therapeutic and tocolysis in multiple gestations [36]. However, judicious use of this therapy is required in every patient but especially for women carrying multiples, as they are at risk for developing complications such as pulmonary edema and cardiac arrhythmias.
- Cervical cerclage – There is too little data to comment on the use of cervical cerclage in high-order multiple pregnancies. The only one randomized study carried by Dor and associates did not find benefit in a prophylactic cerclage in twin pregnancy [37]. It is also worth to mention that this surgical procedure carries potential risks for both the mother and her fetus, so cerclage placement for multiple gestation is generally reserved for women with either a strong history or objectively documented cervical incompetence.
- Antibiotics – Although effective in the setting of PROM, there is no role for broad-spectrum antibiotics therapy to prolong latency in preterm labor with intact membranes [38].

Intrauterine Growth Restriction (IUGR)

Intrauterine growth restriction occurs more frequently in twins and higher order multiple gestations than in singleton pregnancy and is a significant cause of increased neonatal morbidity and mortality. IUGR in multiple pregnancies is a radiological diagnosis that requires either an estimated fetal weight (EFW) <3rd percentile (2 standard deviations from the mean) for gestational age or an EFW <10th percentile for gestational age along with evidence of fetal compromise (usually oligohydramnion or abnormal umbilical artery Doppler velocimetry) [39, 40]. Of course, accurate gestational age dating is clearly critical for the diagnosis. Alexander et al. clearly show that until the 27th week no difference is present between birth weights of singletons, twins or triplets. At 28 weeks, however, birth weight of twins and triplets starts to lag behind that of singletons, with little difference between twins and triplets until 32 weeks [39]. This apparently normal decrease in growth rate in twin pregnancies after 28 weeks has been attributed to placental crowding and anomalous umbilical cord insertion. It is indicated that neonatal morbidity (meconium aspiration syndrome, hypoglycemia, polycythemia, pulmonary hemorrhage) may be present in up to 50% of IUGR neonates [40-42]. Long-term studies show a twofold increase.
in the incidence of cerebral dysfunction (ranging from minor learning disability and cerebral palsy) in IUGR infants delivered at term, and an even higher incidence if infant was born preterm [43]. Principles of management include identification of women at risk, early antepartum diagnosis, attempts to identify etiology, regular fetal surveillance, and appropriate timing of delivery.

Fetal Growth Discordance (defined as a 20% difference in EFW between fetuses of the same pregnancy) is a marker of growth abnormality and is associated with an increased risk of fetal death and neonatal mortality of morbidity. It is evident in 5% to 15% of twins and 30% of triplets and is associated with six-fold increase in perinatal morbidity and mortality. Significant risk factors for discordant growth include monochorionic placentation, preeclampsia and antepartum bleeding [44]. Principles of management are the same as for IUGR.

Premature Rupture of Membranes (PROM)

PROM refers to rupture of the fetal membranes before the onset of labor or before 37 week of gestation. Preterm PROM complicates 2-4% of singleton and 7% to 10% of twin pregnancies. It is associated with 30 to 40% of preterm births and 10% of all perinatal mortality [45]. One of the major risk factors include prior PROM (recurrence risk is 20-30%), unexplained vaginal bleeding, placental abruption (seen in 10-15% of women with PROM, but may be a result rather than cause), cervical insufficiency, vaginal and/or intravenous infection, amniocentesis, smoking, polyhydramnios and chronic steroid treatment. In multiple pregnancies, PROM typically occurs in the presenting sac, but it can occur in the non-presenting twin, especially after invasive procedures such as amniocentesis.

The period from PROM to delivery is dependent on several factors:

a. gestational age (at term 50% of women with PROM go into spontaneous labor within 12 hours and 95% within 72h; latency is generally longer if PROM occurs preterm with 50% of women going into labor within 24-48h and 70-90% within seven days [46].

b. severity of oligohydramnios (severe oligohydramnios is associated with shorter latency period) and number of fetuses (twins have shorter latency period than singletons) [3, 47, 48].

Neonatal complications are related primarily to prematurity, including respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC) and sepsis. Overall PROM is associated with a four-fold increase in perinatal mortality and a three-fold increase in neonatal morbidity [31, 48]. Maternal complications include increased cesarean delivery, intravenous infection and postpartum endometritis. The largest study which looked at the outcome after PROM in twins versus singleton pregnancies concluded that perinatal and neonatal outcome were similar in the two groups; however the median latency period was significantly shorter in twins (12.4 versus 19.5 hours) [49]. Another study reported that chorioamnionitis as well as advanced inflammation was significantly lower in the non-presenting as compared with the presenting twin, but only in dichorionic placentas [50]. Discordant infection in twins may be important since the fetal inflammatory response syndrome is associated with an increased risk of impaired neurologic outcome, however, this has not been systematically studied in twin pregnancies [51, 52].

The management of PROM should not differ significantly in twin as compared with singleton pregnancies. It should include documentation of fetal wellbeing, exclusion of intravenous infection, broad-spectrum antibiotic therapy to prolong latency, avoidance of tocolytics and antenatal corticosteroids [53-55].

Hypertensive disorder of pregnancy

Hypertensive disorders of pregnancy are one of the main complications of multiple gestation; these include hypertension induced by pregnancy and preeclampsia. According to Newman and Luke, hypertension induced by pregnancy in twin gestation account for 14%, in triplets 21% and quadruplets even 41% [56]. Hypertensive disorders of pregnancy are the second most common cause of maternal death in the United States (behind thromboembolism), accounting for 15-20% of all maternal deaths [57, 58]. It actually increases the risk for the mother of pulmonary embolism and stroke, which can be even 3 to 12 times greater during third trimester as well as during labor and puerperium [59]. Hypertension is also associated with high perinatal mortality and morbidity rates, primarily due to iatrogenic prematurity.

Most adverse event occurring in the setting of preeclampsia, Preeclampsia (gestational proteinuric hypertension) is an idiopathic multisystem disorder complicates 68% of all pregnancies [57, 58]. Both pregnancy-induced hypertension and preeclampsia are more common in women carrying twins. A secondary analysis of a large prospective multicenter trial of women with twins (n=684) and singleton (n=2946) pregnancies designed to investigate the efficacy of low dose aspirin for the prevention of preeclampsia was done by Sibai et al. Rates of gestational hypertension and preeclampsia were twice as high as compared with singleton pregnancies (13% vs 5-6%). In addition, early severe preeclampsia and HELLP syndrome were seen more frequently with multiple gestations [60].

The diagnosis, management and course of gestational hypertension are not usually affected by the fetal number. However, multiple gestation with PIH requires close care often associated with hospitalization. Overall, the recommendations associated with management of multiple gestation are known. Still, since the risk of IUGR as well as preterm delivery increases, it is required to have much closer and more frequent surveillance of the fetus and the mother.

Recommendation for care include collection of a precise gynecologic and obstetric medical history which includes knowledge of the conception (spontaneous or assisted), chronicity, previous deliveries, previous operations, weight gain, history of uterine contractions, monitoring of blood pressure as well as history of any chronic diseases of the circulatory,
The greatest problems are associated with the second twin controversial subjects is mode of delivery in twin pregnancies. One of the most risk of delivering premature neonates. induced by pregnancy and twin-to-twin transfusion syndrome. It is essential to make sure that the patient is aware of the risk of complications, which may appear during pregnancy. Properly set visitsshould allow early detection of cervical dilatation, premature labor, hypertension induced by pregnancy and twin-to-twin transfusion syndrome. Early treatment and the patient cooperation may decreases the risk of delivering premature neonates.

Mode of delivery in twin pregnancy

Multiple pregnancies are at a higher risk than singletons for both prenatal morbidity and mortality. One of the most controversial subjects is mode of delivery in twin pregnancies. The greatest problems are associated with the second twin and exist especially in the vertex-vertex presentations. Opinions regarding the mode of delivery have been changing over the decades. Prior to 1970, the route of delivery of twin gestations was dictated by the presentation of the first twin; with delivery of the first twin complete, maneuvers then considered appropriate to deliver the second twin included internal podalic version and complete breech extraction [61]. Taylor in 1976 suggested a cesarean delivery for all twins with malpresentation of the second twin regardless of fetal weight [62]. Others recommended that vaginal delivery, irrespective of the position of the second twin, is valid as long as the fetal weight is >1500 g and the gestational age is ≥32 weeks [63, 64]. Because of the existing controversy, multiple retrospective studies and one randomized study have been conducted to determine the best mode of delivery, which would decrease the mortality and morbidity among twins [64, 65]. Unfortunately, not even one of these studies has reached a final answer. It is presently agreed that delivery should be based on individual needs and may depend on the clinician's practice and experience. In case of vertex-vertex presentation in twin pregnancies, it is anticipated that vaginal delivery is appropriate in such cases.

**Twin A-Vertex with Twin B-Vertex.** According to recent literature, vertex/vertex twins should be delivered vaginally. Several large studies show no increase in neonatal morbidity and mortality when twins were allowed to deliver vaginally [21, 66-68]. Most authors agree that vaginal birth is appropriate for vertex/vertex twins born after 33 week or weighing at least 1500 to 2000 g. The American College of Obstetricians and Gynecologists in their educational bulletin states that vaginal birth is appropriate for vertex/vertex twin gestations unless there are specific contraindications to vaginal birth [70]. Cesarean delivery should be performed for the same indications applied for singleton gestations.

**Twin A-Vertex with Twin B-Nonvertex.** This presentation accounts for approximately 35% of twins and represents one of the major areas of controversy among obstetricians. Present recommendations regarding delivery of twins in such presentation are not clear. The literature contains mostly retrospective and one randomized study, but all failed to reach final answer and do not permit formulation of a policy for delivery. Rabinovici, based on his randomized study, stated that the neonatal outcome of twins with vertex/breech or vertex-transverse presentation after the thirty-fifth week of gestational age was not significantly influenced by the route of delivery [64]. Other authors suggested that it is reasonable to allow labor and vaginal delivery, irrespective of the presentation of the second twin as long as the fetal weight is >1500 g and the gestational age ≥32 weeks [63, 71, 72]. Apart from all these findings, the rate of cesarean sections is significantly increasing with the main indication being malpresentation in twin pregnancy. Due to the fact that the second twin is at a significant disadvantage, most of the obstetricians make their decisions trying to avoid complications [73]. In the view of many practitioners experienced in the management of labor and

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**Table 1. Significant risks associated with twin pregnancies**

<table>
<thead>
<tr>
<th>Obstetric complications</th>
<th>Risks*</th>
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<tbody>
<tr>
<td>Anemia</td>
<td>× 2</td>
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<tr>
<td>Pre-eclampsia</td>
<td>× 3</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>× 4</td>
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<tr>
<td>Antepartum hemorrhage</td>
<td>× 2</td>
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<tr>
<td>Postpartum hemorrhage</td>
<td>× 2</td>
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<tr>
<td>Fetal growth restriction</td>
<td>× 3</td>
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<tr>
<td>Preterm delivery</td>
<td>× 6</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>× 2</td>
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</tbody>
</table>

*Compared with singleton pregnancies

**Table 2. Complications associated with twin pregnancy**

<table>
<thead>
<tr>
<th>Uteroplacental complications</th>
<th>Fetal complications</th>
</tr>
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<tbody>
<tr>
<td>Placental abruption</td>
<td>Intrauterine growth restriction</td>
</tr>
<tr>
<td>Cord entanglement</td>
<td>Congenital anomalies</td>
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<tr>
<td>Placenta previa</td>
<td>Twin-to-twin transfusion syndrome</td>
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<tr>
<td>Preterm premature rupture of membranes</td>
<td>Fetal growth discordance</td>
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<tr>
<td>Postpartum hemorrhage</td>
<td>Intrauterine fetal demise of one or both twins</td>
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<td></td>
<td>Malpresentation</td>
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<tr>
<td></td>
<td>Twin reversed arterial perfusion (TRAP) syndrome</td>
</tr>
</tbody>
</table>

Cesarean section × 2
Preterm delivery × 6
Fetal growth restriction × 3
Postpartum hemorrhage × 2
Fetal growth restriction × 2
Cesarean section × 2

**Opinions regarding the mode of delivery have been changing over the decades.** Prior to 1970, the route of delivery of twin gestations was dictated by the presentation of the first twin; with delivery of the first twin complete, maneuvers then considered appropriate to deliver the second twin included internal podalic version and complete breech extraction [61]. Taylor in 1976 suggested a cesarean delivery for all twins with malpresentation of the second twin regardless of fetal weight [62]. Others recommended that vaginal delivery, irrespective of the position of the second twin, is valid as long as the fetal weight is >1500 g and the gestational age is ≥32 weeks [63, 64]. Because of the existing controversy, multiple retrospective studies and one randomized study have been conducted to determine the best mode of delivery, which would decrease the mortality and morbidity among twins [64, 65]. Unfortunately, not even one of these studies has reached a final answer. It is presently agreed that delivery should be based on individual needs and may depend on the clinician's practice and experience. In case of vertex-vertex presentation in twin pregnancies, it is anticipated that vaginal delivery is appropriate in such cases.
delivery, substantial numbers of twins in this presentation will present with serious acute intrapartum problems following the delivery of twin A, including cord prolapse, prolonged interval to delivery of twin B, birth trauma, risk of emergency cesarean section, prenatal death and neonatal mortality [74, 75]. Additionally, a policy of planned vaginal birth is associated with 30-40% rate of emergency cesarean section. Even among those twins in which twin A is delivered vaginally, there is still a 7% risk of the mother needing to deliver twin B by emergency cesarean section. Considering the risk of maternal death, which is the highest if delivery is by emergency cesarean section, the obstetrician has to think about planned vaginal birth or planned cesarean section in order to be prepared for complications, which may occur during delivery.

Twin A – Nonvertex. In general, cesarean section is the method of choice when the first twin is nonvertex, such as breech or transverse presentation. In pregnancies of greater then 24 weeks, most authors agree with cesarean section as a preferred route of delivery, basing their decision on the increased rate of complications associated with vaginal delivery such as interlocking twins which occurs 10 times more frequently in breech/vertex than in vertex/breech [76]. In this type of collision, the percentage of prenatal neonatal and fetal death is between 43 and 72%, depending on the type of collision, and it mainly concerns the first twin [77].

Fetal morbidity and mortality in the aspect of mode of delivery

The literature indicates that the increased number of cesarean sections performed for twins with low birth weight didn’t cause significant changes in the frequency of cerebral palsy nor did it decrease the risk of stillbirth [78-80]. In addition, it failed to have any significant impact on the long-term development of twins with different birth weights and increase in the morbidity and mortality of second twins. Most authors agree that the follow up of neurodevelopment and psychomotor development at the end of first year of life does not indicate differences between children born as first and second [81, 82].

Interval between birth of twins

In the past an interval between twins of more than 30 minutes was considered as an factor which increases morbidity and mortality in the second twin by reducing the uterine-placental circulation [83]. The optimal time for this interval was 10 to 20 minutes. Earlier delivery <10 min was associated with increased frequency of intrapartum injury and what followed increased mortality of the second twin [83, 84]. In addition, a longer interval than 20 minutes was not indicated because it was supposed to lead to intrauterine fetal hypoxia. Some authors had a different point of view; in four studies which were performed in 1980 with continuous electronic fetal monitoring there was no increase in morbidity and mortality related to an increased interdelivery time period [85-88]. In one of these studies, Rayburn et al. indicated that there was no difference in fetal acidemia or base excess in those delivered at fewer than 30 min or greater than 30 min after the first twin [83]. Nowadays, in most of the developed countries the time interval of more than 1 hours is rather rare. At a time when continuous fetal and uterine monitoring is possible, the time interval between delivery of twin A until the time of delivery of twin B has no practical significance. However, the clinician should always think about the remaining fetus and the time interval should be limited by the risk of possible complications.

Optimal delivery timing

The optimal timing of delivery for twin pregnancy is when the health care provider and his/her team can deliver two healthy infants. It has been long thought that multifetal pregnancies achieve maturity earlier than fetuses of singleton gestation. Underlying this statement with evidence that preterm infants of multifetal pregnancies achieve better outcomes than infants of singleton pregnancies, there is also evidence that optimal prenatal outcome occurs earlier and at lower birth weight in multifetal pregnancies than in singleton pregnancies. Luke reported that in the United States the lowest fetal death rates in twin pregnancies occurred at 36 to 37 weeks of gestation and at 40 to 41 weeks of gestation in singleton pregnancies [89]. The most recent study by Hartley suggested that the optimal gestational age for twin delivery is 37 to 38 weeks of gestation, indicating that during this time the rates of prenatal mortality, RDS and long hospital stay are the lowest [90]. Considering these facts, induction of labor at 37 to 38 weeks of gestation should be routinely considered in twin pregnancy.

Anesthesia in twin gestation

The decision about anesthetic techniques when it comes to cesarean section should be considered individually for every patient according the anesthesiologic and obstetric risk. Looking at the literature it is evident that whether the cesarean section is performed under emergency or elective conditions, the use of regional anesthesia should be considered. Regional anesthetic techniques include epidural and subarachnoid blockade. Some authors avoid the latter based on an increased incidence of hypotension [91, 92]. The use of regional type of anesthetic technique has benefits for the mother as well as the fetus. The mother is able to stay conscious, breathe by herself, which protect her from the risk of aspiration and hypoxia. In addition, it supports her hemodynamic stability much better than in case of general anesthesia. Additionally it stabilizes and even improves the blood flow through placenta, which in case of hypotension induced by pregnancy or preeclampsia protect the fetuses from hypoxia [93]. More so, especially during premature deliveries, it eliminates the fetal exposition to harmful drugs, which are injected during the general anesthesia.

It is now recognized that there is increased maternal mortality rate associated with general anesthesia in singleton pregnancies and theoretically further increases in multiple pregnancies [94, 95]. The larger uterus encroaches to a greater degree upon the functional residual capacity, increasing hypoxemia in the supine position. An unfavorable shift in the angle of the lower esophageal sphincter increases the likelihood of regurgitation of gastric contents, which can result in
aspiration pneumonia. There is an increased incidence of postoperative vomiting. In addition, general anesthesia has been associated with poor outcome in second twin. All of these factors support the avoidance of general anesthesia.

The use of general anesthesia for abdominal delivery of twins is indicated when:

- There is absolute contraindication to regional anesthesia (severe thrombocytopenia, tumor of spinal cord, significant spinal deformity);
- In cases where immediate delivery is required and epidural anesthesia is not in place (e.g., fetal distress).

Neurodevelopment of children from twin pregnancy

The neurodevelopment of neonates from twin pregnancies is mainly influenced by the premature birth of these children, their prematurity as well as low and very low fetal weight at the same time contributing to higher rates of mortality, morbidity and long-term disability compared to singleton pregnancy. Around 50% of newborns from twin pregnancies are born prematurely, and this is the main factor, which increases the risk of developmental problems in these children. The rapid progress in the field of neonatology and neonatal intensive therapy has been followed by a decrease in perinatal morbidity and mortality. However, these improvements have also a considerable negative side. Specifically, due to the ability to save children from multiple pregnancies with very low birth weight, increased numbers of children with developmental disabilities are being seen. Children from twin pregnancies have greater risk of future developmental complications than children from singleton pregnancies. Neonates associated with the greatest risk of complications are the ones with fetal weights under 1000 g (increased risk of intraventricular hemorrhages), monzygotic twins (especially monozygotic monoamnionic) and neonates from pregnancy where death of one fetus took place, in which the risk of cerebral palsy in the second twin increases by 15 times.

Clinically, the neurodevelopmental complications mainly include an increased risk of cerebral palsy which is 12 times greater than in singleton pregnancy [96, 97]. The most common form of palsy in twins is spastic diplegia. Other neurological disorders include disabilities of hearing, sight, gait and speech. In general, the prognosis in cases of severe disability can be made after the second year of life, whereas disorders of mild to moderate degree may not be fully detected until 5 to 7 years of life. In 12% children from twin pregnancies, careful observation can detect learning difficulties, speech disability, dysgraphia and dyslexia. There is also close association between children with slow development and low birth weight and prematurity.

Among the numerous unanswered questions, concerning multiple pregnancy is the mode of delivery, both in terms of the outcome and the further development of the neonate. The Twin Birth Study is an international multicenter randomized study, which is trying to answer this question by comparing the planned vaginal delivery to planned cesarean section for twins at 32-38 weeks of gestation.

References

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