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### REVIEW PAPER



## Multiple pregnancy - overview

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### Abstract

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**Introduction:** Pregnancy with more than one fetus in uterus is not a physiological phenomenon for a woman. The risk of most of pregnancy complications is higher and there is a possibility of abnormalities, which are not met in singleton pregnancy, caused by having two or more fetuses supplied by one placenta.

**Aim:** Author analyzed recent literature regarding up-to-date management of multiple pregnancy and recommended time and mode of delivery.

**Material and methods:** Recommendations regarding management of multiple pregnancy in available guidelines of gynecological societies and national healthcare institutions were analyzed. Latest articles from Pubmed describing current views on multiple pregnancy management and delivery options were also reviewed.

**Results and discussion:** Guidelines for multiple pregnancies management, including delivery time and mode planning, were analyzed and compared. Most of them are very consistent, there are only few differences in recommended pregnancy management. Diagnosing pregnancy complications as early as it is possible and adequate treatment is the aim of pregnancy management, and as multiple pregnancies have higher risk of all complications, they have to be monitored very closely. Diagnosis of type of pregnancy, routine follow-up visits schedule and ultrasound scan scheme are discussed as well as the recommended time and mode of delivery. Vaginal delivery for well defined group of patients should be considered, while cesarean section seems safer for some women.

**Conclusions:** Multiple pregnancies, as high risk pregnancy, require more frequent visits and ultrasound scans depending on chorionicity and amnionicity. Close monitoring and careful qualification for vaginal delivery improves pregnancy outcome.

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### **1. INTRODUCTION**

Pregnancy with more than one fetus in uterus is not a physiological phenomenon for a woman. The risk of most of pregnancy complications is higher and there is a possibility of abnormalities, which are not met in singleton pregnancy, caused by having two or more fetuses supplied by one placenta.<sup>1-4</sup> That's why all multiple pregnancies, regardless the type of gestation, should be managed in referral centers by experienced specialists. Follow-up should be closer, more visits should be scheduled and range of procedures at every visit is different for different types of multiple pregnancy. Planning time and mode of delivery is also crucial to minimize the risk of perinatal complications.

## 2. AIM

Author analyzed recent literature regarding up-to-date management of multiple pregnancy and recommended time and mode of delivery.

## **3. MATERIAL AND METHODS**

Recommendations regarding management of multiple pregnancy in available guidelines of gynecological societies and national healthcare institutions were analyzed. Latest articles from Pubmed describing current views on multiple pregnancy management and delivery options were also reviewed.

## 4. RESULTS AND DISCUSSION

Guidelines for multiple pregnancy management of Polish Ministry of Health and Polish Society of Obstetricians and Gynecologists<sup>4–7</sup> as well as worldwide societies like FIGO<sup>2</sup> or ISUOG<sup>8</sup> and national societies and institutions in Great Britain,<sup>910</sup> France,<sup>11</sup> Canada<sup>1,12,13</sup> and United States<sup>14</sup> were analyzed and compared.

There are two main mechanisms of multiple pregnancy origination. Single egg cell fertilization with later splitting (monozygotic gestation) or multiple fertilizations in one menstrual cycle (dizygotic gestation) may result in multiple gestation. Describing multiple pregnancy we describe not only its zygosity, but also chorionicity (number of placentas) and amnionicity (number of amniotic sacs).

Zygosity means the number of fertilized egg cells. In dizygotic pregnancy (fraternal twins) every embryo has different set of genes, similarities between children is like between siblings born from two separate pregnancies. Dizygotic pregnancy is always dichorionic – every fetus has its own placenta. Monozygotic pregnancy originates from one fertilized egg cell which splits into two or more embryos. Children in this type of pregnancy are identical. Depending on the time of splitting gestation may be dichorionic (during first 3 days) or monochorionic (after 3<sup>rd</sup> day), monochorionic gestation may be diamniotic (4<sup>th</sup>-7<sup>th</sup> day) or monoamniotic (8<sup>th</sup>-13<sup>th</sup> day). Late splitting (after 13<sup>th</sup> day) results in conjoined twins. Monochorionic pregnancy is unique situation with more than one fetus supplied by one placenta, where communication between both fetuses is present in anastomoses (communicating vessels).

Incidence of multiple pregnancy is increasing mostly due to more frequent use of assisted reproduction and increasing age of reproduction. In natural conception it depends on the race and family tendency, and is reported to be 1.5%–3.0%.<sup>3</sup>

Increased risk of all pregnancy complications observed in multiple gestation results in increased frequency of intrauterine deaths (approximately 5-fold) and neonatal mortality (7-fold). The most important for clinicians and the most frequent multiple gestation complication is preterm delivery. Types and risk of complications depend on chorionicity and amnionicity, thus defining them at the earliest opportunity is always emphasized.<sup>1,2,4–6</sup>

### 4.1. MANAGEMENT OF MULTIPLE PREGNANCY

Diagnosis of multiple pregnancy and its type should be completed at 12–14 weeks of gestation, at the 1<sup>st</sup> trimester ultrasound scan. At this gestational age assessment of chorionicity and amnionicity is the most reliable and its accuracy decreases with gestational age. Chorionicity and amnionicity warrants planning of follow-up visits for pregnant woman.<sup>4</sup> Markers of chorionicity and amnionicity are presented in Table 1.

Verification of the gestational age, important in planning delivery, at the first trimester scan is also the most precise.<sup>5</sup>

## Table 1. Assessment of chorionicity and amnionicity of twin pregnancy in ultrasound examination.

Tupo of programou	Dichariania	Monochorionic	
Type of pregnancy Dichorionic		Diamniotic	Monoamniotic
Number of gesta- tional sacs	Two	One	One
Numer of yolk sacs	Two	Two	One
Dividing mem- branes thickness	Thick >1.8 mm	Thin <1.8 mm	Absent
Dividing mem- branes placental attachement	Lambda sign	Tau sign	Absent
Fetal sex	The same/ different	The same	The same

Regardless the type of multiple pregnancy every woman should be examined vaginally every 2–4 weeks to prevent preterm delivery and to diagnose too early ripening of the uterine cervix. Ultrasound measurement of uterine cervix at 18–22 weeks is usually recommended to assess the risk of preterm delivery and to diagnose short cervix.<sup>1,2,4,8,10,11,13</sup> Canadian guidelines suggest even repeating the measurement at 23–24 weeks.<sup>1</sup> Frequency of visits and ultrasound scans beyond 16 weeks depend on the type of pregnancy.

### DICHORIONIC PREGNANCY

Prenatal visits should be scheduled every 2–4 weeks according to the guidelines. Special attention should be paid to the symptoms of the most frequent complications of multiple pregnancies – preterm delivery and gestational hypertension including preeclampsia.<sup>1,2,4,8–12,14</sup>

Ultrasound monitoring of the fetuses' growth should be more frequent than in singletons in the second half of pregnancy, usually it is recommended every 4–6 weeks. More frequent scans are dictated by higher risk of fetal growth restriction (FGR) and it's complications (fetal hypoxia and intrauterine death). Early detection of FGR improves pregnancy outcome.<sup>1,2,5,8-10,13,14</sup>

Fetal growth in multiple pregnancy from 28–20 weeks of gestation becomes slower than in singletons. There are growth charts prepared specifically for twins available on internet. It is recommended to use them when examining twins,<sup>5</sup> but they are not included in ultrasound units software what would make it much easier for sonographers. Canadian guidelines state, that it is acceptable to use growth charts for singletons, and it doesn't affect twin pregnancies outcome.<sup>13</sup>

Fetal growth restriction diagnosis as not clear, was a subject of Delhi procedure.<sup>16</sup> Consensus of this procedure regarding FGR diagnosis for dichorionic and monochorionic pregnancies is presented in Table 2.

Table 2. Algorithm 1	for diagnosis of feta	growth restriction
in twins according t	o results of Delphi p	rocedure.

Pregnancy type	Monochorionic	Dichorionic
Solitary	EFW of one twin <3 <sup>rd</sup> centile	EFW of one twin <3 <sup>rd</sup> centile
Contributory	EFW of one twin <10 <sup>th</sup> centile	EFW of one twin <10 <sup>th</sup> centile
	EFW discordance >25%	EFW discordance >25%
	UmA PI of smaller twin >95 <sup>th</sup> centile	UmA PI of smaller twin >95th centile
	AC of one twin <10 <sup>th</sup> centile	
Algorithm for contributory para- meters	Three out of four	Two out of three

Comments: EFW – estimated fetal weight; PI – pulsatility index; AC – abdominal circumference.

#### Table 3. Differentiation of monochorionic twins complications by ultrasound symptoms.

Complication	Ultrasound symptom
sFGR	EFW discordance
TTTS	MVP discordance
TAPS	PSV MCA discordance

Comments: sFGR – selective fetal growth restriction; EFW – estimated fetal growth; TTTS – twin-to-twin transfusion syndrome; MVP – maximal vertical pocket; TAPS – twin anemia-polycythemia sequence; PSV MCA – peak systolic volume in middle cerebral artery.

### MONOCHORIONIC PREGNANCY

Monochorionicity and monoamnionicity increase the risk of pregnancy complication more than just multiplicity of gestation. All pregnancy complications are more frequent in monochorionic pregnancy when compared to dichorionic, but there are some specific complications of monochorionic gestation. They include twin-to-twin transfusion syndrome (TTTS), selective fetal growth restriction (sFGR) and twin anemia-polycythemia sequence (TAPS). Table 3 presents the symptoms differentiating these complications. Twin reversed arterial flow (TRAP) may be diagnosed by finding a fetus without visible heart and reversed blood flow in umbilical artery – from placenta to the fetus.

In monochorionic pregnancy prenatal visits should be scheduled every 2–3 weeks or every 3–4 weeks after 16 weeks according to most guidelines.<sup>1,2,4,5,8–11,13,14</sup> Ultrasound scan with biometry, amniotic fluid measurement and doppler ultrasound is recommended every 2 weeks. In women with high risk of TTTS or sFGR ultrasound scans should be scheduled even every week. The high risk markers are: intertwin clown-rump length (CRL) discordance greater than 20%–25% or 6 mm, nuchal translucency (NT) difference above 20% or 2 SD, tricuspid regurgitation, absent or reversed 'a' wave in ductus venosus (DV) in one of the twins, discordant umbilical cord insertions or discordant amniotic fluid volume with both maximal vertical pockets (MVP) within normal range found in the first trimester scan.<sup>5</sup>

Ultrasound scan in monochorionic pregnancy includes assessment of maximal vertical pocket of amniotic fluid (MVP), bladder filling, peak systolic velocity in middle cerebral artery (PSV MCA), pulsatility indices (PI) in MCA and umbilical artery (UmA), tricuspid, ductus venosus and umbilical vein (UV) blood flow regardless how frequent they are performed. Biometry should be performed biweekly. Monitoring EFW will enable detection of sFGR – early (before 24 weeks of gestation) or late (after 24 weeks). Measurement of PSV MCA is recommended to screen for hemoglobin discordance between fetuses to diagnose TAPS. Discordance in MVPs (≤2 cm in donor and ≥8 cm in recipient) is the symptom of TTTS.<sup>1,2,4,5,8–11,13,14</sup> There are guidelines suggesting echocardiography at 20–22 weeks in multiple pregnancy, some of recommendations suggest it for all monochorionic gestations, some save it for pregnancies with suspected TTTS.<sup>1,8</sup>

In monoamniotic twins using amniotic fluid volume to screen for TTTS is impossible. This complication is diagnosed only after reaching the second Quintero stage where no urine is visible in urinary bladder of donor, or after developing doppler abnormalities typical for stage 3 TTTS – pulsatility in UV, increased PI in UmA, absent or reversed flow in DV.<sup>17</sup> Other pathologies (TAPS, TRAP, sFGR) have the same symptoms like in diamniotic pregnancy.

Cord entanglement is a complication exclusive for monoamniotic twins. It is the reason of recommended hospitalization and close monitoring of monoamniotic pregnancy from 26 weeks to the end of gestation. Close monitoring includes weekly ultrasound scan for symptoms of other pathologies of monochorionic twins, but also CTG and biophysical profile monitoring for symptoms of compression of umbilical cords. According to all guidelines, 32–34 weeks is the gestational age, when the risk of neonatal death due to prematurity becomes lower than the risk of sudden intrauterine fetal demise due to cord entanglement, and cesarean section should be performed at this time.<sup>1,24,9</sup>

### **TRIPLETS AND MORE**

Management of triplet pregnancy and pregnancy with higher number of fetuses, regardless chorionicity and amnionicity, is usually planned like in monochorionic diamniotic twins. The exception is situation with at least two monoamniotic fetuses – pregnancy should be followed like monoamniotic twins.<sup>10,14</sup>

### 4.2. DELIVERY OF MULTIPLE PREGNANCY

Choice of time of delivery in multiple pregnancy is conditioned by perinatal mortality caused by prematurity, and by intrauterine fetal deaths increasing with gestational age much earlier than in singleton pregnancies. According to most recommendations depending on the type of twin pregnancy delivery should be scheduled between 32 and 38 weeks of gestation.<sup>1,2,4,5,8–14</sup> Summary of detailed guidelines is presented in Table 4.

According to most guidelines delivery of dichorionic twins should be planned at 37–38 weeks of gesta-

# Table 4. Recommended time of delivery in relation to typeof twin pregnancy

Type of twin pregnancy	Recommended time of delivery, weeks
Dichorionic	37–38
Monochorionic diamniotic	36–37
Monochorionic monoamniotic	32–34

tion. Delivery of monochorionic diamniotic twins are usually scheduled approximately a week earlier, at 36–37 weeks of gestation. In patients qualified for vaginal delivery it is time of induction of labor. In cases of ineffective induction it can be repeated or delayed, but it should not prolong beyond 40 weeks.<sup>12,4,5,8–14</sup>

Monoaminotic pregnancy should not be continued beyond 32–34 weeks due to high risk of intrauterine deaths caused by umbilical cords entanglement.<sup>1,2,4,5,8–14</sup>

Vaginal delivery of diamniotic twins (regardless chorionicity) is the choice for patients with vertical presentation of the first twin, and the estimated fetal weight (EFW) of the second twin not much higher than EFW of the first one. There is no influence of the second twin presentation on the rate of cesarean section on the second twin after vaginal delivery of the first one. Once the first one is born, external or internal version may be safely and quickly performed if needed, usually much faster than organizing cesarean section. Non-vertex presentation of the first twin or bigger second twin are indications for planned cesarean section. The EFW difference is not always precised, it is usually described as 'much bigger,' or defined as 20%–25% or 500 g difference.<sup>1,2,4,5,8-14</sup>

Other pregnancy complications, like for example severe preeclampsia, are indications for cesarean section like in singleton pregnancy, having twins does not change counseling. Careful qualification for vaginal delivery, considering all possible contraindications resulting from twin pregnancy, maternal and fetal factors, decreases the risk of cesarean section on the second twin after vaginal delivery of the first one to as low as 4%.<sup>18</sup>

Delivery of triplets starts usually spontaneous, most frequently before 36 weeks, but should be ended with cesarean section. If it doesn't start earlier, cesarean section should be planned at 36–37 weeks.<sup>10,14</sup>

Summarizing, indication for cesarean section in multiple pregnancy are:

- (1) non-vertex presentation of the first twin;
- (2) big EFW difference with the second twin bigger than the first one;
- (3) monoamniotic pregnancy;
- (4) pregnancy with more than two fetuses.

## 6. CONCLUSIONS

Most of analyzed guidelines are consistent regarding multiple pregnancy management and delivery planning. Due to high risk of complications of these pregnancies dependent on the type of gestation, follow-up is much closer than in singletons and based on the type of gestation. Frequent visits and targeted ultrasound scans enable detecting of most of multiple pregnancy complications early. Prompt diagnosis, like with many other diseases, is an unquestioned condition of effective treatment and improvement of pregnancy outcome.

Safe birth of multiplets depends on carefully chosen time and mode of delivery. It is essential to explain the patient why the particular time and mode of delivery is the safest for her children to provide maximal cooperation of pregnant woman.

### CONFLICT OF INTEREST

None declared.

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None declared.

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