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REVIEW ARTICLE

Multiple Pregnancy under Ultrasound Umbrella

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ABSTRACT

Multiple pregnancy care based only on knowledge of fetal number does not satisfy clinical practice any more. Appropriate clinical use of data obtained via skilled and timely ultrasound has been proven to be of great value for reduction of typical complication rate in multiple pregnancy for both fetus and mother. Ultrasonography plays a key role when intrauterine interventions during pregnancy are required. It can be successfully used for both precise prenatal diagnosis of numerous chromosomal and congenital diseases and antenatal treatment of multiple pregnancy-specific complications, so medical professionals should be well-trained and experienced. And it is impossible without everyday clinical work, gaining individual knowledge and skills and being informed on developments and achievements in the best world recognized perinatal centers.

Keywords: Multiple pregnancy, Ultrasonography, Multiple pregnancy-specific complications, Intrauterine interventions.

INTRODUCTION

Multiple pregnancy is a pregnancy when two or more fetuses develop in a mother's womb. Heterotopic pregnancy with one or more embryos developing outside uterine cavity is also called multiple pregnancy. Also, any type of multiple pregnancy is a high-risk one *vs* singleton cases. Due to significant deterioration of perinatal outcomes comparing with singleton pregnancies, every type of multiple one is considered as pathology.

International disease classification (IDC) codes for multiple pregnancy:

O30 — Multiple pregnancy
O30.0 — Twin pregnancy
O30.1 — Triplets pregnancy
O30.2 — Quadruplets pregnancy
O30.8 — Other multiple gestation
O30.9 — Multiple gestation, unspecified
O31 — Complications specific to multiple gestation
O31.0 — Papyraceous fetus
O31.1 — Continuing pregnancy after abortion of one fetus or more
O31.2 — Continuing pregnancy after intrauterine death of one fetus or more
O31.8 — Other complications specific to multiple gestation

Almost two decades have passed since the 10th ICD review and many fundamental disease classification features (as we can see for multiple pregnancies) are not exhibited in ICD-10, but will certainly appear in subsequent editions.

Epidemiology

As a matter of fact, multiple pregnancy prevalence is determined with the number of twins deliveries. For many centuries in different regions it depended mainly on two factors: Increased prevalence with higher average age of pregnant women and their previous birth number. By the end of the 1970s, the multiple pregnancy prevalence in Europe decreased sharply owing to strong parity fall. That moment it was ranging from 9 to 12 cases per 1000 deliveries (1% of all deliveries). The rate of triplets and high-order multiples was less than 0.001% and did not significantly affect the overall multiples prevalence in general population. Recent decades showed rapid (200%) multiple pregnancy prevalence increase caused with distinct increase of average mother age and, most significantly, widespread advance of assisted reproduction technologies (ART) accompanied with multiple pregnancy rate amounting to as much as 20 to 35%.[1,2]

Pathogenesis

Natural cycle multiple pregnancy develops either out of several oocytes (heterozygous twins—2/3 of multiple pregnancy cases) or from one oocyte divided on early gestation stages (homozygous twins—1/3 of multiple pregnancy cases). The homozygous twin type depends on the day of division and is determined with so-called "4 day rule"; if the oocyte divides within first four days (Days 0-4) after fertilization at zygote morula stage, dichorionic multiple pregnancy develops (1/3 of cases). Division during next four days (Days 4-8) at early blastocyst stage results in monochorionic diamniotic pregnancy (2/3 of cases). And embryoblast division at another four days (Days 8-12), when the amnion has been already formed, brings forth monochorionic monoamniotic pregnancy (1%). In case of 12 to 13 days division, conjoined twins develop. The latter event prevalence is one per 40,000 deliveries (0.5% of monozygotic multiple pregnancies).

Post-ART incidence of heterozygous multiples is about 10 to 14 cases per one monozygotic pregnancy. However, considering high multiple pregnancy prevalence in these women, the monozygotic pregnancy rate and related specific complications in general population has substantially increased.

Classification

Multiple pregnancy classification according to IDC-10 is based on delivered fetuses' number. However, perinatal outcomes of multiple pregnancies (even twin pregnancy) are determined not by number of fetuses but by the twins type. In this case, twins zygosity has no significant perinatal value, whereas chorionicity and amnionicity determine the whole range of potential complications specific for multiple pregnancies.

Decrease of chorionicity and amnionicity values relatively to the developing fetus number increases perinatal complication rate placing multiple pregnancy at the group with extremely high perinatal risk.

Clinical and anatomical classification of multiple pregnancy (using twin pregnancy as an example):

- Dichorionic diamniotic twin pregnancy (either mono- or dizygotic, same or different fetal gender);
- Monochorionic monoamniotic twin pregnancy (always monozygous and always same fetal gender);
- Monochorionic monoamniotic conjoined twins (it is always monozygotic and always same fetal gender, despite possible absence of genitals in one of them)

This classification method is also applicable to triplets and high-order multiples (Figs 1 to 3).

Diagnostic Ultrasound

Appropriate clinical use of data obtained via skilled and timely ultrasound has been proven to be of great value for reduction of typical complication rate in multiple pregnancy for both fetus and mother. And multiple pregnancy is one of the most vivid examples. Ultrasonography plays a key role when intrauterine interventions during pregnancy are required. It can be used for both prenatal diagnosis and antenatal treatment of multiple pregnancy-specific complications. Along with that, making decision concerning management of a particular multiple pregnancy case requires the whole battery of existing ultrasound methods: Transabdominal, transvaginal, 2D and 3D real-time procedures, prenatal echocardiography and encephalography, Doppler evaluation of uterine, placental and fetal blood flow and variety of invasive diagnostic procedures.[2,3]

First Trimester Ultrasound

Spontaneous multiple pregnancy should be diagnosed early in the first trimester. The 11 to 14 weeks ultrasound screening has 100% sensitivity and specificity even at primary level.

In case of induced pregnancy the probability of iatrogenic multiples is very high. Proper time for diagnostic procedures is 6 to 8 weeks of gestation as per obstetrics rather than embryologic calculations. At this time even ordinary ultrasound equipment is able to detect number of fetal eggs and fetuses. Also, it can visualize embryo cardiac activity and rule out heterotopic pregnancy. If multiple pregnancy is found in ART or maternity clinics, such patients should be referred to secondary level facilities for ultrasound examination regardless of gestational age at the time of detection.

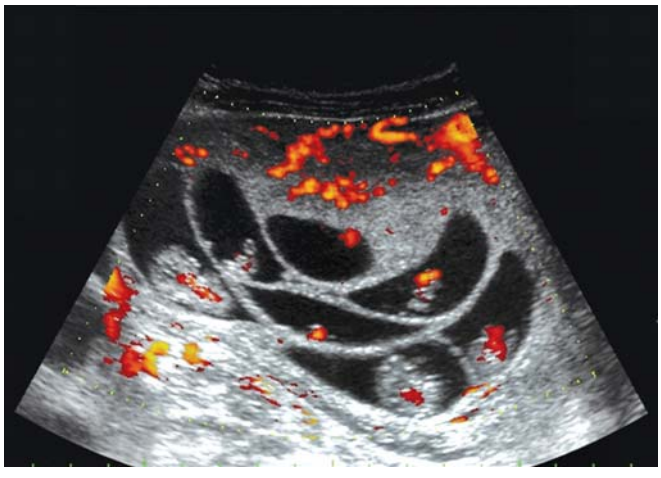


Fig. 1: Septumchorionic septumamniotic septuplets

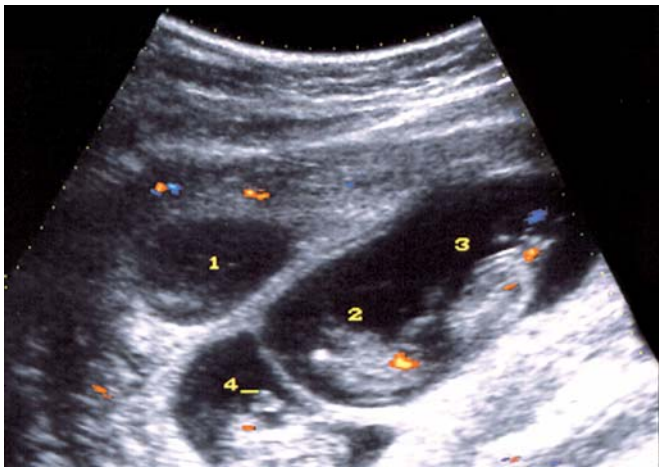


Fig. 2: Trichorionic triamniotic quadruplets

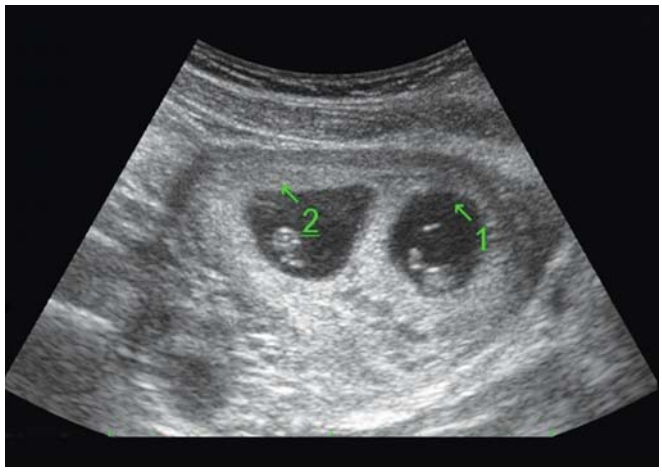


Fig. 3: Early dichorionic diamniotic twins

Secondary level ultrasonography in the first trimester of multiple pregnancies should answer several questions and exclude some abnormal conditions. It determines future pregnancy management and perinatal outcomes.

The issues to be resolved are as follows:

- Quantity of gestational sacs in uterus
- Quantity of fetuses in uterus
- Quantity of fetuses with cardiac activity
- Chorionicity
- Amnionicity
- Heterotopic gestational sacs location
- Current gestation age
- Fetal malformations
- Ultrasound markers of chromosome disease
- Intrauterine mass lesions
- Uterus malformations, concomitant myometrium and ovary disorders
- Cervix and internal os evaluation.

Based on the data obtained multiple pregnancy should be mapped, recording its particular features. Compulsory referral of the patient with multiple pregnancy to a tertiary level does not preclude possibility of accurate ultrasound diagnostics on the primary level. It would rather serve to improvement of primary level physician skills. However, finalizing diagnosis and compiling specific recommendations for further pregnancy management should be tertiary clinic domain.

Quantity of Gestational Sacs and Number of Fetuses in Uterus

Gestational sacs in the uterus by transvaginal ultrasound can be detected even just after the 4th week of gestation. It is well known that the number of identified gestational sacs (GS) in the uterus at uncomplicated pregnancy does not often correspond to the number of newborns. This discrepancy has two possible explanations. First, there are diagnostic mistakes after transabdominal ultrasound. In such cases, GS can be considered as retrochorionic hematomas or fluid accumulating in retrochorionic space. Second, there is the "vanishing twin" phenomenon. Thus, detection of two GS leads to twin newborn delivery in 80%. If three GS are detected, triplets are born only in 60%. If the GS number is above three the same number of newborns are delivered just in 50%. The "vanishing twin" incidence rises in line with mother age, post-IVF procedures and in initially monochorionic cases. Transvaginal ultrasound at the 6th week of gestation can show embryo and yolk-sac in the GS cavity. This timeframe also suits completely to multiple pregnancy. Though usually transabdominal approach increases this timing by one week. Except monoamniotic multiple pregnancies the number of yolk-sacs should correspond to the number of embryos (Figs 2 to 4).

Quantity of Fetuses with Cardiac Activity

Embryo's heartbeat can be recorded at 6th or 7th week of gestation. The best method for recording and heart rate assessment is B and M modes combination. In this case, color Doppler should be used with caution because of the unproven but potentially possible negative effect on the further fetal development. However, if *heterotopic pregnancy* is suspected the color Doppler technique is essential for early and accurate identification of GS location. It is also crucial to confirm continuous pregnancy development shaping further management decisions (Fig. 1). At the 6 to 7th week of gestation, embryo's heartbeat is about 70 to 90 bpm. It gradually increases to 160 to 180 bpm by 10 to 11th weeks and then decreases to 140 bpm by 15 to 16th weeks. After 16th week this parameter averages and remains the same until delivery.

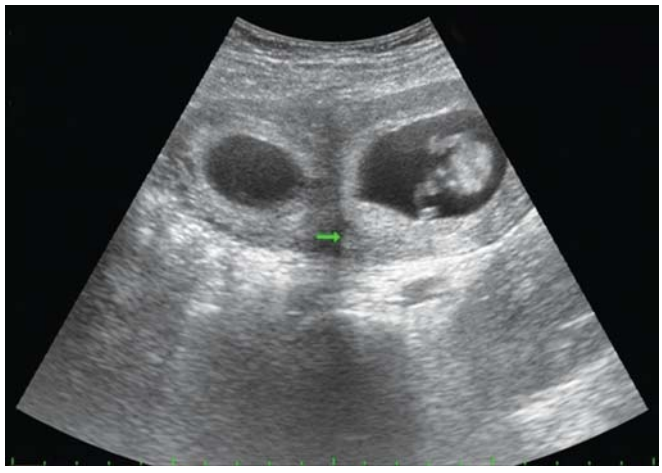


Fig. 4: Vanishing twin phenomenon in dichorionic diamniotic pregnancy

Multiple Pregnancy Chorionicity and Amnionicity

Effective perinatal care in multiple pregnancy is impossible without timely identification of its chorionicity. Timely identification with regard to ultrasound means high sensitivity and specificity of the method with provision of low degree of false-positive and false-negative results at the decision making point. Chorionicity can be determined already at the 4th week of gestation with transvaginal ultrasound. Multiple pregnancy is diagnosed identifying several 2 to 5 mm hypoechogenic rounded structures with clear internal contour and hyperechoic rim in decidual tissue. However, at this time it is possible to identify di- or higher-chorionic pregnancies rather than monochorionic multiples making ultrasound insufficient in clinical sense. Prior to the 6th week, GS cavity is presented with celomic cavity located between chorion and amnion. Only by the 7th gestational week, amniotic cavity starts to enlarge and at the 8th week amniotic membrane can be visualized as a linear hyperechoic structure on the border between celomic and amniotic fluids. Thus, it makes possible to evaluate pregnancy amnionicity. And by the 9th week of gestation, a set of ultrasound signs of chorionicity and amnionicity allow to describe multiple pregnancy type. Presence of two or more embryos with registered heartbeat and separate amniotic cavities

and chorions located in different uterus parts are the grounds to diagnose dichorionic diamniotic twins. Absence of membranes between embryos can confirm monoamniotic pregnancy with high reliability even at this time point (see Figs 2 and 3). Much more difficulties occur with regard to differential diagnostics of diamniotic monochorionic and dichorionic pregnancy with "joined" chorion. The end of the first trimester is optimal for visualization of membrane structures in the chorionic plate contiguity. Such differential diagnostics is based on conventional "λ" and "T" signs. "λ" indicates dichorionic multiple pregnancy and "T" indicates monochorionic one (Fig. 4). If ultrasound equipment has high resolution, it is possible to determine the number of amniotic membrane layers. If there are four, the multiple pregnancy is dichorionic; if there are two, it is monochorionic[3,4] (Figs 7 to 10).

Heterotopic GS Localization

This pathology incidence is about 0.003 to 0.007%. In most cases infertility is caused by uterine tubes diseases. Its surgical correction or tubectomy does not eliminate but sometimes even increase heterotopic pregnancy risks. IVF transfer of more than

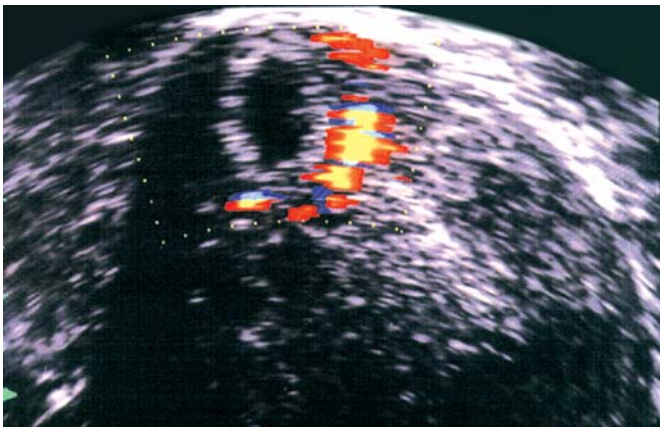


Fig. 5: Early interstitial pregnancy

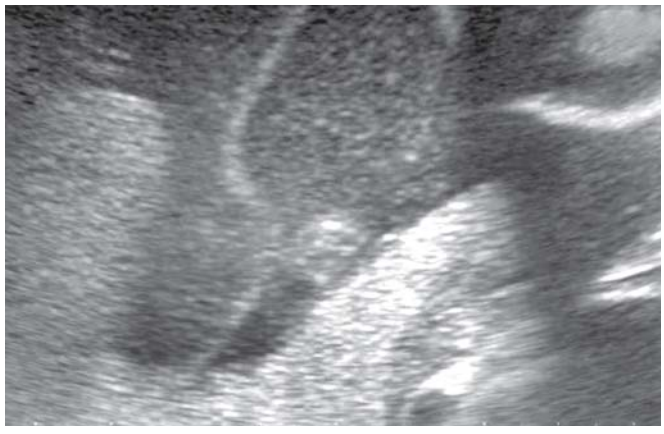


Fig. 8: "T"-sign in monochorionic pregnancy

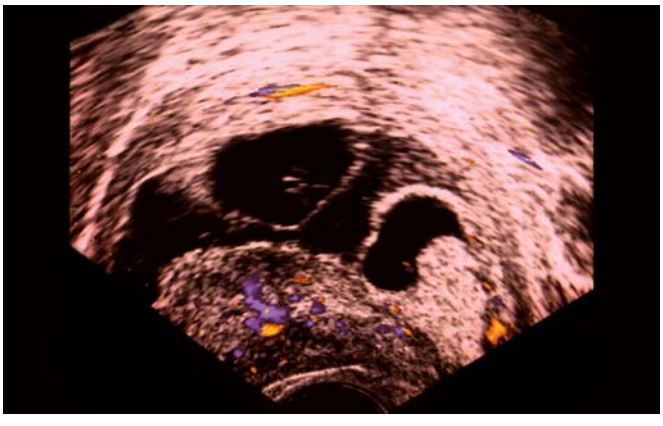


Fig. 6: Early isthmus-cervical heterotopic pregnancy along with intrauterine pregnancy

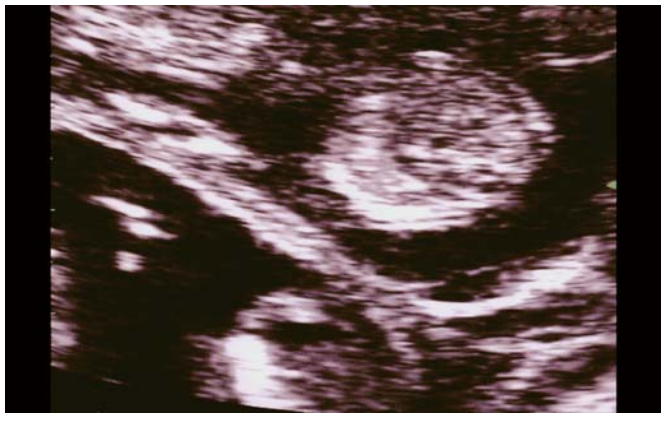


Fig. 9: Four leaves of interamniotic membranes in dichorionic diamniotic twins

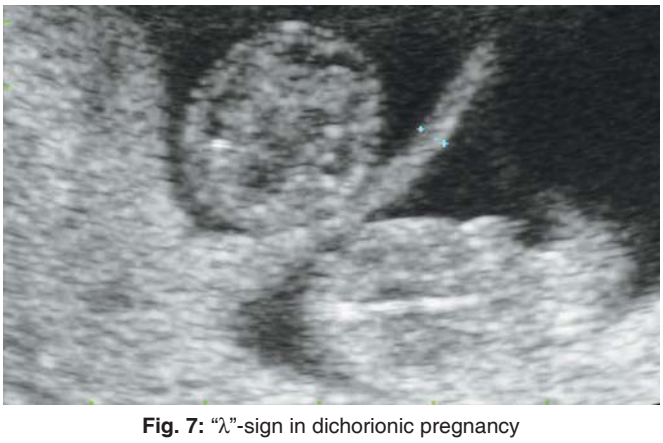


Fig. 7: "λ"-sign in dichorionic pregnancy

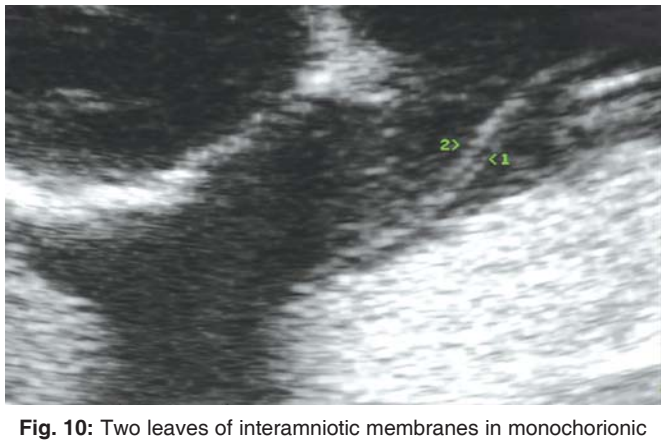


Fig. 10: Two leaves of interamniotic membranes in monochorionic diamniotic twins

one embryo is associated with 150- to 300-fold increased incidence of heterotopic pregnancy and reaches the rate of 1 to 1.5%. Ultrasound diagnostics of ectopic GS implantation within myometrium may be not a big issue for an experienced specialist. However, if normal GS is detected in uterine cavity, it is sometimes very hard to find another GS of heterotopic location. And sometimes in such cases without proper vigilance it is even impossible. Thus, only catastrophic clinical complications of heterotopic pregnancy can bring forth the right diagnosis (Figs 5 and 6).

Current Gestational Age

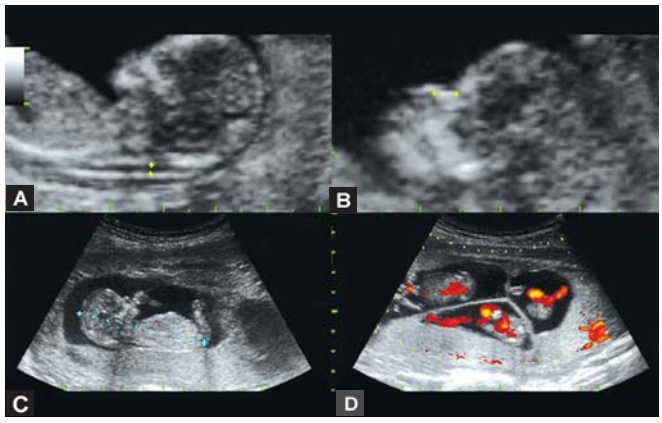
It should be quite clear that with regular menstrual cycle obstetric gestational age starts countdown from the first day of the last period. So, we can talk about 280 days, 9 lunar months and 40 weeks of gestation. Not all women have regular menses. In such cases we can take ovulation or follicle puncture day, deduct 14 days and the obtained day will be the zero day of gestation. Numerous studies showed that absolute mistake of CRL-based assessment of gestational age in the first trimester does not exceed 3 to 5 days. In twin pregnancy arithmetic mean of two CRL's is calculated providing similar accuracy with insignificant absolute error increase. In triplets, one day is to be added to the gestational age value calculated as CRL arithmetic mean of the smallest and the largest fetuses. Quadruplet pregnancy is so rare that the need for gestation age evaluation is hardly of clinical issue. And if the menstrual gestation age differs by less than 5 days from ultrasound one, the real gestational age is presumed to be calculated based on last period date. If it differs by more than 5 days, the gestational age calculation should be based on CRL data.[6]

Fetal Malformations

Modern ultrasound machines can determine malformations at early stages of fetal development. It seems reasonable to substitute term "defect" with "malformation". The main point will not change but will significantly affect the way patients and their partners perceive the problem that later can be successfully resolved especially with timely and highly qualified prenatal counseling. Uncorrectable malformations identification remains a basic ultrasound objective at the first trimester regardless of the fetus number. It is extremely important for multiple pregnancies given capabilities of current invasive diagnostic and therapeutic interventions.[2-4]

Ultrasound Markers of Chromosomal Disease

Prenatal diagnostics in single and multiple pregnancies is based on nuchal translucency. Recently, the following new ultrasound markers of chromosomal diseases are widely discussed: Nasal bone visualization and measurement, facial angle, absent or retrograde blood flow in ductus venous at atrial contraction, tricuspid regurgitation. Along with blood chemistry screening data it determines indications for prenatal karyotyping. The foregoing fully applies to the issue of chromosomal abnormality identification in multiple pregnancy fetuses[2,3,7] (Figs 11A to 14).



Figs 11A to D: Fetal ultrasound evaluation in trichorionic triamniotic triplets. (A) nuchal translucence thickness measurement, (B) nasal bones visualization and measurement, (C) CRL measurement, (D) heart beat visualization

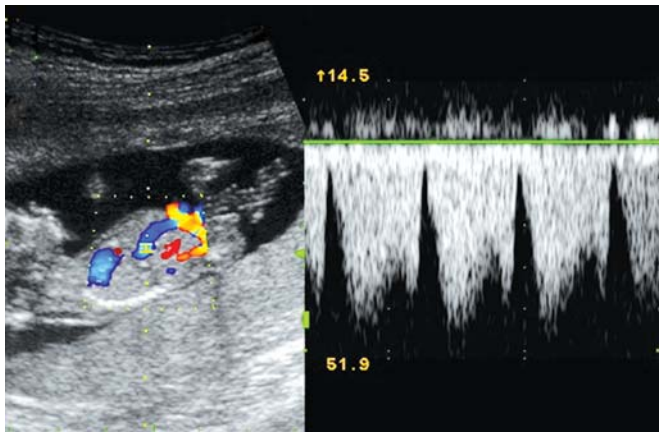


Fig. 12: Normal Doppler blood flow in the first trimester fetus—orthograde blood flow during whole cardiocycle

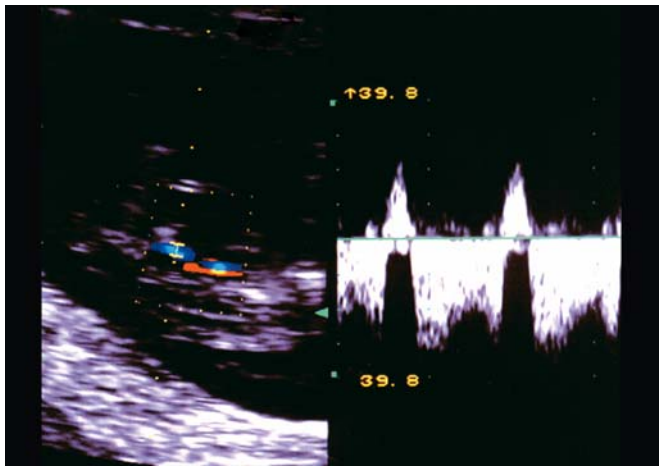


Fig.13: Retrograde blood flow velocity waveforms from the ductus venosus at atrium contraction phase

Intrauterine Mass Lesions

Significant intrauterine mass lesions in multiple pregnancy include retrochorionic hematoma caused by decidual tissue

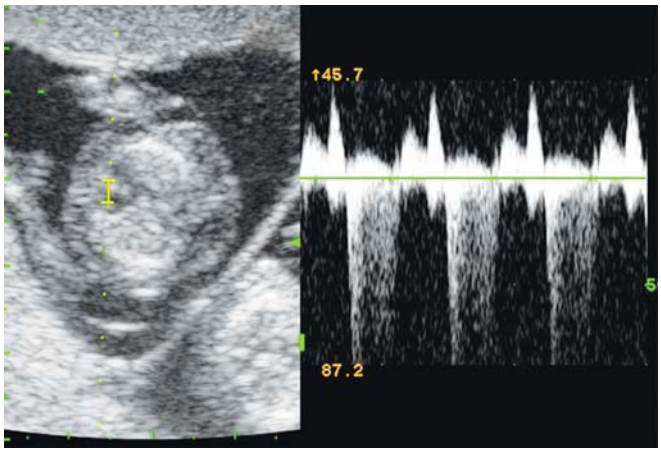


Fig. 14: Doppler sign of tricuspid valve blood flow regurgitation

bleeding if a living embryo is present. It leads to chorionic leave dislocation from uterus wall (Fig. 6). In case of embryo death, it is caused with villous chorion detachment and myometrial spiral artery bleeding. Retrochorionic hematoma increases the risk of unfavorable pregnancy outcomes but doesn't determine it for either singleton or multiple pregnancy.

Uterus Malformations, Concomitant Myometrium and Ovary Disorders

Ultrasound diagnostic principles for uterus malformations do not differ from those of single pregnancy. In this case, 3D-ultrasound can be of help and simplifies lesion visualization. If uterus malformations have been noted, uterus cavity/cavities should be examined carefully to rule out heterotopic multiple pregnancy. In case of post-ART pregnancy, ovary's biometric parameters are to be assessed taking into account possibility of hyperstimulation syndrome that can complicate pregnancy course.

Cervix and Internal os Evaluation

Ultrasound assessment of cervix and internal os is important for early heterotopic pregnancy detection. Currently clinical value of ultrasound cervicometry for preterm delivery risks in the first trimester for either singleton or multiple pregnancy still remains unclear.

Ultrasound in the Second and Third Trimester of Multiple Pregnancy

If fetus number corresponds to the number of placentas and amnions, ultrasound diagnostics is not different from the one for singleton pregnancy. Chorionicity assessment in these periods is impossible in multiple pregnancy, since T-signs disappear. In such situation if you are not sure about the chorionicity type, it makes sense to consider that pregnancy is monochorionic and recommend appropriate ultrasound and clinical monitoring.

Growth Rate and Fetus State Assessment in Multiple Pregnancy

Birth weight in multiple pregnancy is significantly lower compared with that in singleton one owing to genetically determined possibility to bear only certain "total fetus weight". Statistical review of large data sets on multiple pregnancy exhibited that birth rate of newborns with birth weight less than 2.500 gm is 6, 52 and 92% for singleton, twin and triplet pregnancy respectively. And differences of fetal weight increase rate in singleton pregnancy *vs* average fetal weight in twin and triplet pregnancies appear only after 28 to 30 weeks of gestation. Differences of average fetal weights in twin *vs* triplet pregnancy are noted only after 35th week of gestation. Assessing ultrasound biometry data, fetal weight dissociation phenomenon in multiple pregnancy should be taken into account. Scientific publications provided 15, 20 and 25% differences of fetal birth weights as markers of unfavorable perinatal outcomes but it is not always true reviewing large datasets for multiple pregnancies. Even in singleton pregnancy differential diagnostics of intrauterine growth restriction (IUGR) and small for gestational age fetus phenotype in some cases is rather complex.[5] Therefore, it is clear that to avoid iatrogenic preterm deliveries without proper grounds ultrasound procedure per se and obtained data interpretation are to be done in tertiary level clinics.

IUGR diagnostics and decisions on various interventions in multiple pregnancy cases are based on similar grounds as for singleton ones. Such grounds are as follows: Expected fetal weight assessment using multiple pregnancy-adapted nomograms. If the difference of fetal weight *vs* its average value is beyond 10 percentiles functional fetal status should be assessed with conventional Doppler technique. Combined with fetal heart rate variability evaluation it can serve nicely in choosing the best way for further pregnancy management.

Amniotic Fluid Assessment in Multiple Pregnancy

In multiple pregnancy amniotic fluid index for each amniotic cavity still is not standardized. That is why for quality assessment the same criteria are utilized. These are as follows: Maximal vertical amniotic pocket measurement for each amniotic cavity and total amniotic fluid index. Biophysical profile score in multiple pregnancy shows low sensitivity and negative predictive value with regard to antenatal fetal death limiting its clinical use.

Cervix Evaluation at the Second Trimester

Transvaginal sonographic cervical length at 20 to 24 weeks' gestation is a good predictor of spontaneous preterm birth in asymptomatic women with twin pregnancies.[10] If cervical shortening is asymptomatic and cervix length is below 20 mm, ultrasound monitoring along with progesterone treatment is widely recommended but not proven. With cervical length of less than 15 mm the use of cervical pessary is becoming more and more popular.

Ultrasound Diagnostics in Monochorionic Multiple Pregnancy

Perinatal mortality rate in monochorionic cases increases three to five times *vs* dichorionic pregnancy. It is caused by specific complications of this multiple pregnancy type.[8,9]

Twin to Twin Transfusion Syndrome (TTTS)

Twin to twin transfusion syndrome (TTTS) is noted in 10 to 30% of all monochorionic pregnancies. In this case perinatal, infant and early neonatal death rate exceeds 80 to 90%. At the same time neurological complications incidence in survivors is very high.

TTTS is caused by development of hemodynamic disbalance with blood transfer from one twin (the donor) to the other (the recipient) through placental anastomoses. Arteriovenous anastomoses play a major role in TTTS pathogenesis. The donor twin develops hypovolemia while the recipient exhibits hypervolemia with further hemodynamic impairments having typical ultrasound signs.

TTTS has five following stages:[11] (1) Oligohydramnios and polyhydramnios (Fig. 15), (2) no bladder visualization in donor twin (Fig. 17), (3) absence or reverse blood flow in donor umbilical artery at diastole phase and/or no or reverse blood flow in recipient venous duct at atrial contraction phase, (4) recipient hydrops as extreme presentation of blood flow failure (Fig. 18), (5) antenatal death of one or both fetuses (Fig. 29).

Timely TTTS diagnosis depends on accurate monochorionic type pregnancy and the syndrome marker detection in the first trimester. They are as follows: T-sign, increased nuchal translucency thickness, reverse blood flow in ductus venous at atrial contraction phase, no chromosome abnormalities, amniotic fluid disbalance, marginal umbilical cord attachment of one or both fetuses.[9] All these signs can predict TTTS development and require on-going ultrasound monitoring every two weeks.

In the second trimester, TTTS and its severity is confirmed with the following signs:

1. Verified monochorionic pregnancy after examination of intertwin membrane and its location with regard to placenta, i.e. T-sign; confirmed similar fetal gender; membrane thickness less of 2 mm or detection of two membrane leaves also indicates monochorionic placentation; irregular placenta echogenicity.

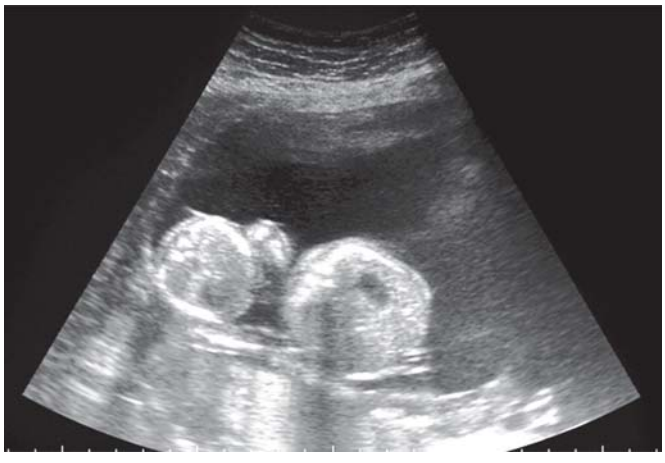


Fig. 15: TTTS in monochorionic diamniotic twins, stuck donor twin and polyhydramnios of recipient twin; growth discordance in twins

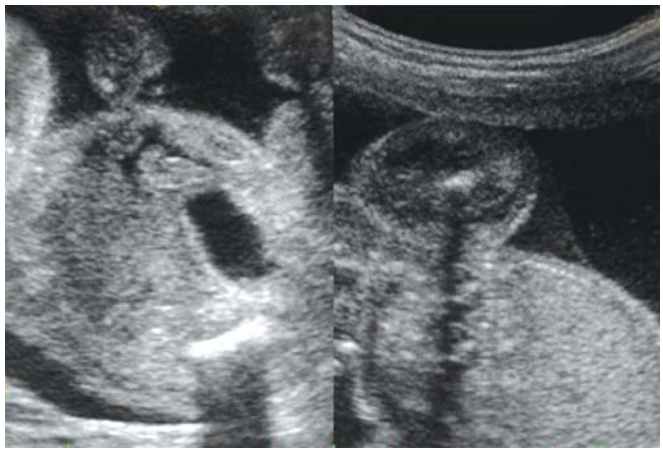


Fig. 17: TTTS—no bladder visualization in donor twin

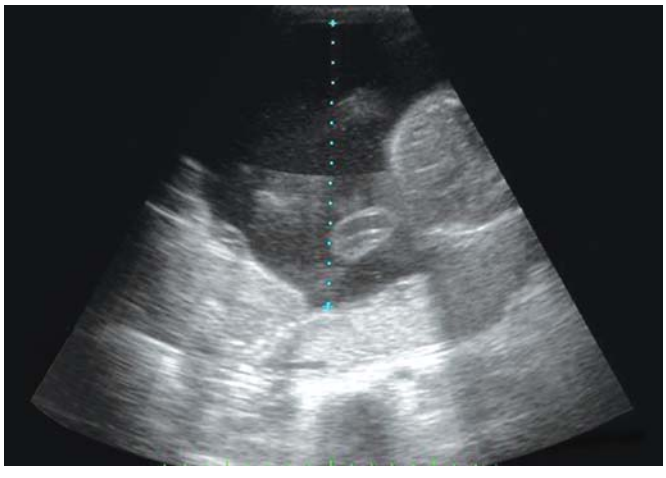


Fig. 16: TTTS—138 mm of maximum vertical amniotic fluid pocket and 463 mm of amniotic fluid index

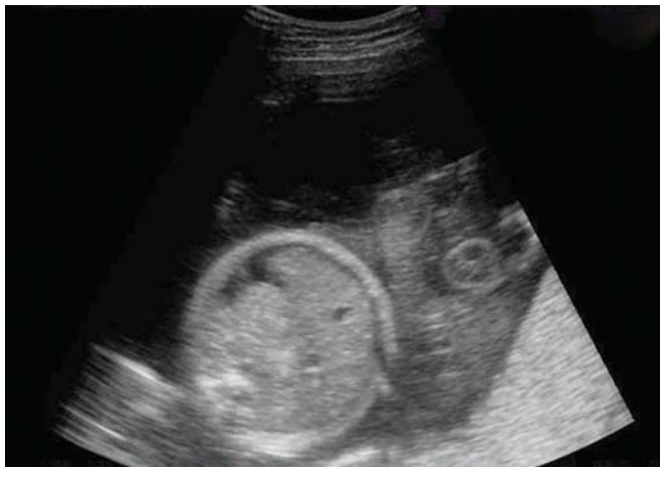


Fig. 18: TTTS—ascites of recipient-twin

2. Amniotic fluid assessment—oligohydramnios and polyhydramnios, decrease of maximum vertical fluid recess below 2 cm in donor twin combined with increase of vertical fluid recess above 8 cm in recipient twin is one of the most important TTTS signs. Stuck and immobile fetus being the TTTS classic sign is found quite seldom. It is often combined with donor twin death in the second trimester beginning. Duplication of donor amniotic leaves surrounding amniotic fluid of recipient fetus is always associated with TTTS.
3. Fetal biometry assessment—TTTS is characterized with fetal estimated weight difference of above 20%.
4. Doppler evaluation of umbilical artery and venous duct blood flow. Increased cardiac after load and/or preload indicate extremely severe TTTS and requires immediate intrauterine intervention or early delivery.[12]
5. Extreme TTTS stages of recipient hydrops or antenatal death of one of the fetuses indicates extremely unfavorable perinatal prognosis.

TTTS Treatment

Treatment methods depend on syndrome severity and gestation age. Amnioreduction (redundant amniotic fluid removal) purpose is to prolong pregnancy up to survival threshold when modern neonatal treatments can provide favorable outcomes for a newborn. This procedure is indicated when maximum vertical amniotic recess is larger than 12 cm and amniotic index is higher than 400. Initially, surgeons tried to remove no more than 1 liter of amniotic fluid considering risks for placenta abruption and uterine contractions. Nowadays, it is preferable to remove as much as possible. Sometimes total volume reaches as much as 10 liters. Sequential amnioreductions in TTTS cases developed prior to 28 weeks increase perinatal survival rate at least for a fetus up to 60 to 70%.[9,11,12]

Laser Coagulation of Fetofetal Anastomoses

Laser coagulation of fetofetal anastomoses is the TTTS treatment method with pathophysiological grounds (Fig. 14). The syndrome development is mainly related to vascular, mainly arteriovenous anastomoses while artery-arterial anastomoses are of some protective value for TTTS development. Selective laser coagulation treatment increased perinatal outcomes for one fetus up to 81 to 83% and decreased neurological complication rate in survival fetus from 24 to only 8%. Though long-term evaluations exhibited that quite high neurological complication rate, about 4 to 9%, despite laser coagulation method used. Comparison of laser coagulation *vs* amnioreduction outcomes showed that the first is preferable. So, now the treatment of choice for TTTS is laser coagulation[13,14] (Figs 19 to 21).

Twin Reversed Arterial Perfusion (TRAP)

This syndrome develops when one of the fetuses in monochorionic pregnancy has no heart, thus, arterioarterial and venovenous anastomoses allow to perfuse blood in it due to contractions of the pump-fetus heart. Prevalence of twin reversed arterial perfusion (TRAP) or acardiac twins is about one in 35,000 deliveries. Syndrome pathophysiology is based on severely impaired fetus heart development and its subsequent total loss

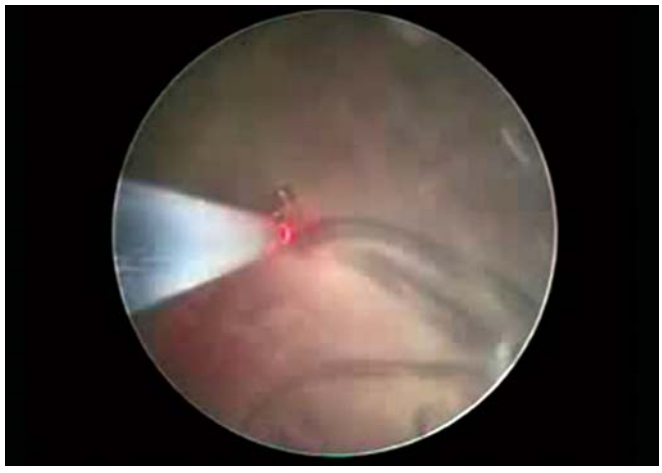


Fig. 19: Laser coagulation of anastomosis in TTTS

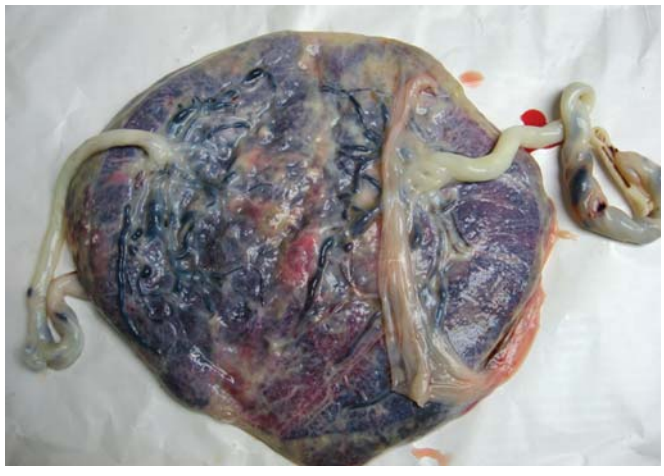


Fig. 20: Monochorionic placenta of TTTS cases after laser coagulation of anastomosis

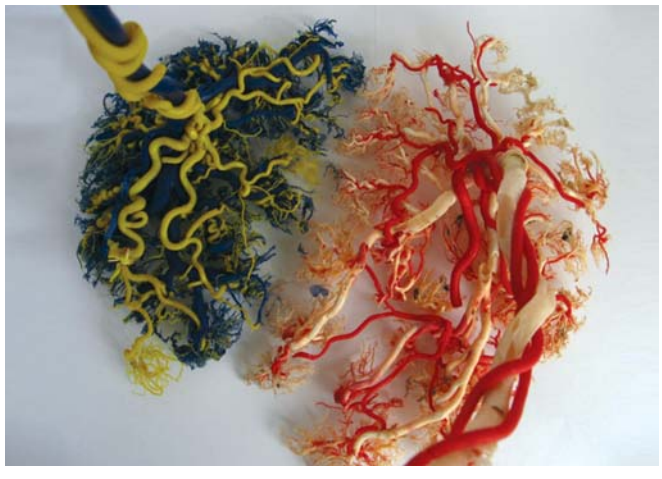


Fig. 21: Placental cast of the same placenta—no communicating anastomosis exist between fetal circulations

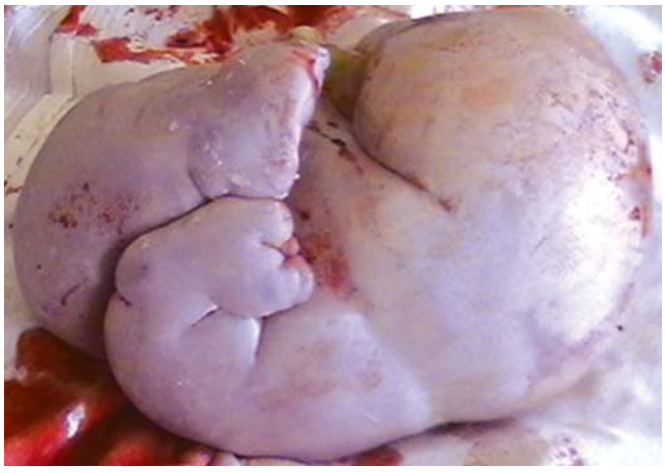


Fig. 22: TRAP—acardiac fetus after delivery

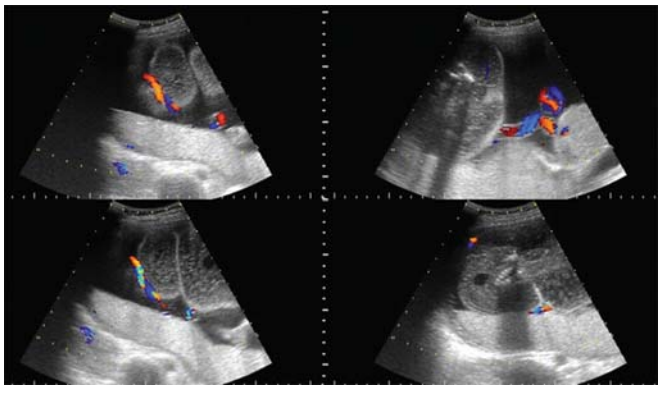


Fig. 23: TRAP—color Doppler blood flow mapping of two vessels umbilical cord of acardiac fetus and three vessels umbilical cord of pump-fetus

if placental anastomoses are present. The acardiac fetus body can be of the following forms: Amorphous – having no anatomical structure; acephalus—legs and pelvic organs are present; aceps—the body is fully formed even with some of facial structures; and acormus—cranial structures are partially formed (Fig. 22). Usually, the second fetus has no malformations, though their chromosome disease rate increases up to 10%.

TRAP can be diagnosed at the end of the first trimester. Its main signs are no heart activity in one of embryos with increase in size of such nondeveloping embryo. Usually, color Doppler shows good blood supply in its tissues[15] (Fig. 23).

Pregnancy management depends on gestation age at the moment of TRAP detection and possibilities for invasive diagnostic and medical interventions. Fetal prenatal karyotyping is indicated. After chromosome abnormalities are ruled out it is possible to manage pregnancy in conservative fashion with obligatory pump fetus monitoring. Pump fetus perinatal mortality rate is about 55%. For monoamniotic TRAP, the monoamniotic twins management protocol is applied considering chances of similar complications. For diamniotic TRAP (noted in 75% of cases) urgent delivery is possible taking into account acardiac fetus size.

Active TRAP management is based on attempt to eliminate acardiac fetus blood supply to prevent pump-fetus heart failure.

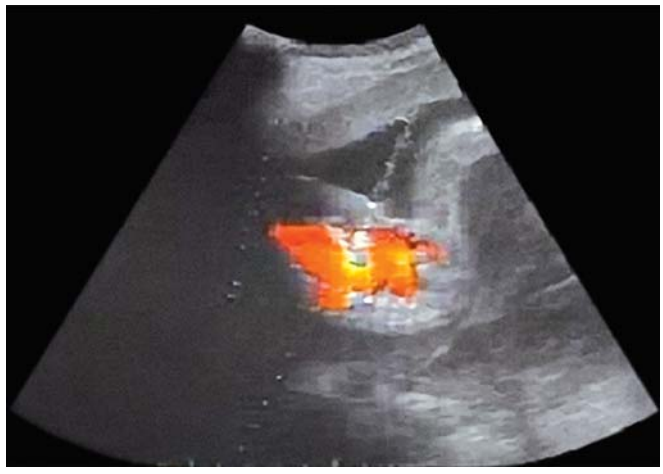


Fig. 24: TRAP—coagulation of main vessels of acardiac twin by laser entered through the puncture needle under ultrasound guidance

Various methods of acardiac fetus umbilical cord occlusion, such as ultrasound-monitored ligation, embolization, laser and diathermal coagulation have been used. Alcohol introduction, laser or diathermal or radiothermal coagulation were tried to occlude main blood vessels in acardiac fetus body (Fig. 24). With such approach pump-fetus perinatal mortality decreased up to 10 to 35% and perinatal outcomes improved for that rare but threatening complication of monochorionic multiple pregnancy.[16]

Monoamniotic Multiple Pregnancy

This pregnancy type can be diagnosed with ultrasonography already in the first trimester. It is based on detection of all monochorionic pregnancy features like single celomic and amniotic cavity with no interamniotic membrane. Single yolk-sac is a clear indication of monoamnionicity that is completely ruled out if two yolk-sacs are present. Since anatomical malformations incidence increases considerably in monoamniotic twins thorough fulfillment of ultrasound protocols is required in both first and second trimesters. High, up to 100%, incidence of umbilical cords collision in monoamniotic twins can lead to sudden deaths of one or all fetuses during pregnancy and delivery. Therefore, cesarean section is a preferable delivery method once fetuses reach survival threshold[18] (Figs 25 and 26).

Conjoined Twins

Ultrasonography diagnosis of conjoined twins is based on the monoamniotic pregnancy visualization failing to find any disconnection between twins bodies and detecting of more than three umbilical vessels. There are publications on both conjoined twins and triplets. Pregnancy management depends on various factors, such as time, place and capacities. But in this case a ultrasound specialist shall not express his opinion with regard to pregnancy management unless he is a member of interdisciplinary team. Postnatal outcomes for conjoined twins can be quite favorable in some cases, at least, for one of them (Figs 27 and 28).

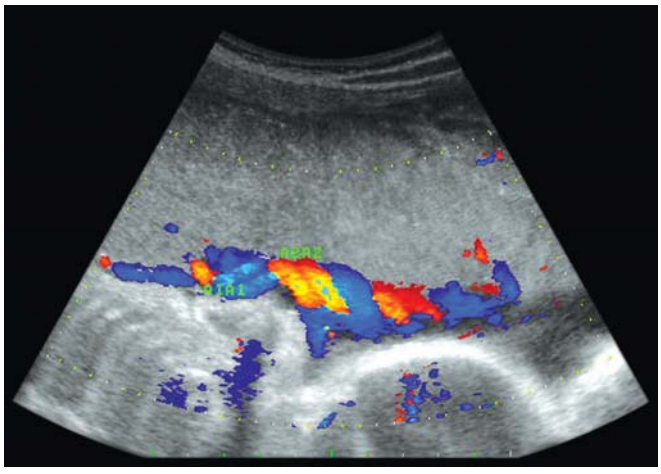


Fig. 25: Monoamniotic twins—umbilical cords collision

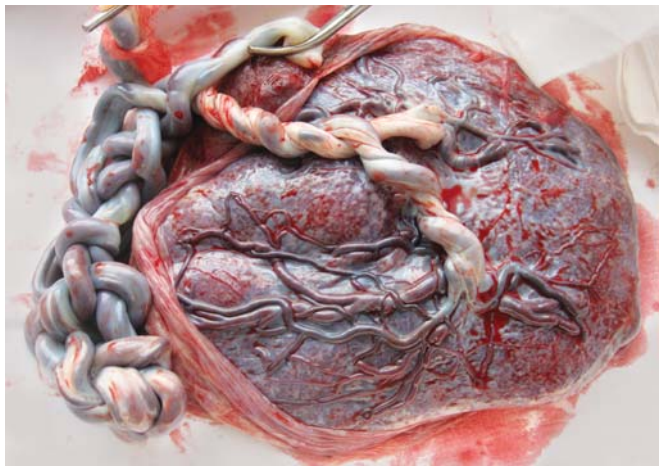


Fig. 26: Monoamniotic twins—placenta and umbilical cords collision after cesarean delivery

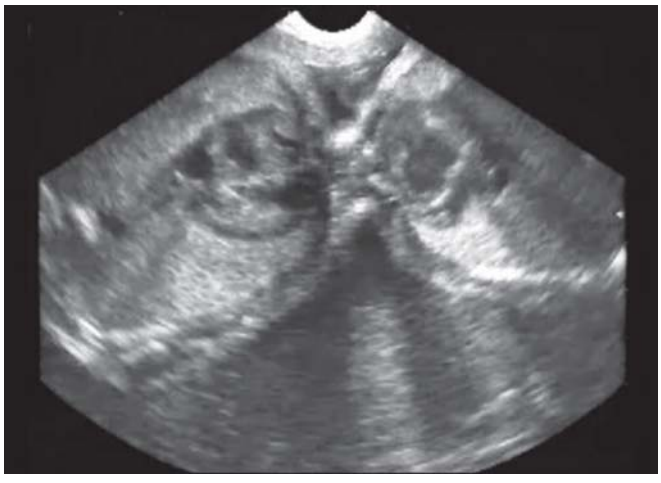


Fig. 27: Thoracopagus—monochorionic monoamniotic twins (*echogram by D Voronin with permission*)

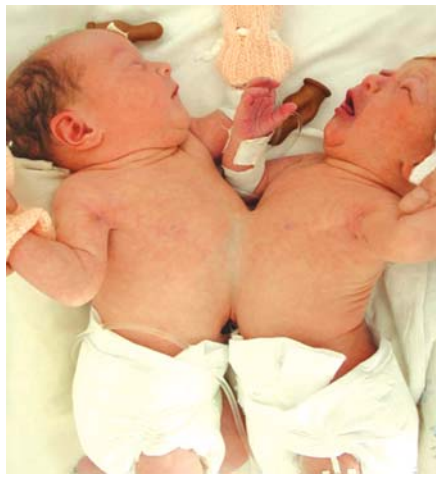


Fig. 28: Thoracopagus before surgery—the same case *(photo by A Mostovoy with permission)*

Ultrasound Diagnostics and Pregnancy Management with One Fetal Death

Ultrasonography in such pregnancy is one of the most important diagnostic methods for chorionicity and pregnancy complication assessment. If pregnancy is dichorionic and one fetus died but the other one shows normal performance any interventions are not considered as justified. If the pregnancy is monochorionic and one fetus is found to be dead before the other one reached survival threshold, pregnancy termination can be considered due to high risk of neurological complications of the survivor (Figs 29 to 31). Comprehensive prenatal neurosonography and MRI can be helpful to justify decision on pregnancy continuation, though sensitivity and false-negative results of these methods have not been established yet .[15]

As a rule, exact time of fetal death is often not known. And if survival threshold of the other twin is reached, expectant management is quite justified. If death time of one of the fetuses is known, emergency delivery is also considered as inappropriate. One fetal death increases risks of antenatal brain lesions in the survivor due to acute anemia and blood pressure collapse after blood shunting via anastomoses to dead fetus circulation. To prevent it, dynamic Doppler monitoring of middle cerebral artery flow detecting severe anemia and brain hypoxia of the living fetus is indicated. Intrauterine transfusion of donor red blood cells can be quite reasonable therapeutic approach.

Ultrasound-guided Diagnostic Interventions in Multiple Pregnancy

Such procedures are mostly performed to rule out fetus chromosomal diseases. Chorionic villus sampling is the only method for the first trimester (Fig. 32). In the second trimester placenta biopsy and amniocentesis are at hand. Method selection is based on cytogenetic laboratory qualification in handling chorion villi and amniocyte samples; time to obtain cytogenetic results; physician experience with these interventions; complication rate after them in a particular clinic; possibility to discern sampling sites as related to the same or different fetuses. Amniocentesis is known to be the safest technique concerning postoperative complications but it is important to remember that in dichorionic multiple pregnancy two amniotic cavities are to be punctured. It increases procedure risk several times *vs* singleton pregnancy. Chorionic villus sampling advantage is shorter time to get cytogenetic report. Nowadays diagnostic

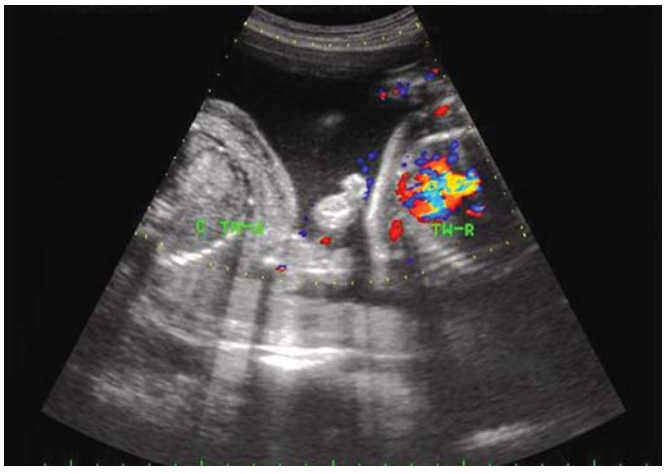


Fig. 29: One fetal death in monochorionic diamniotic twins

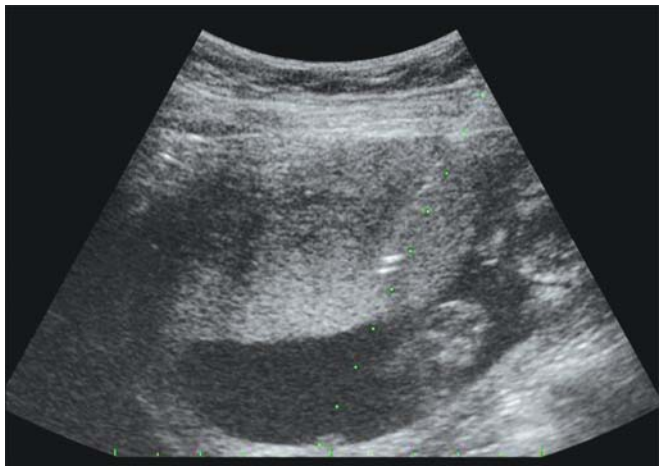


Fig. 32: Chorionic villus sampling in multiple pregnancy

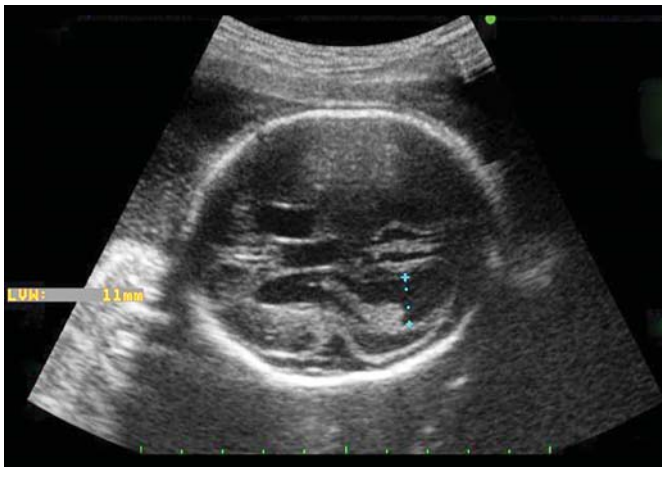


Fig. 30: One fetal death in monochorionic diamniotic twins: The same case after two weeks—progressive ventriculomegaly of alive twin

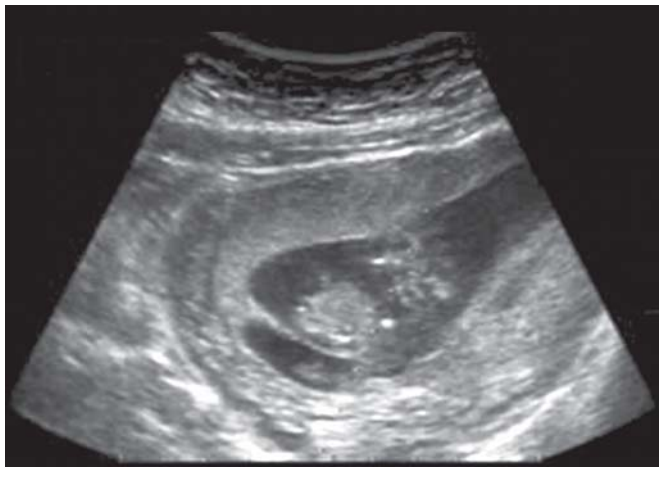


Fig. 33: Multifetal pregnancy reduction

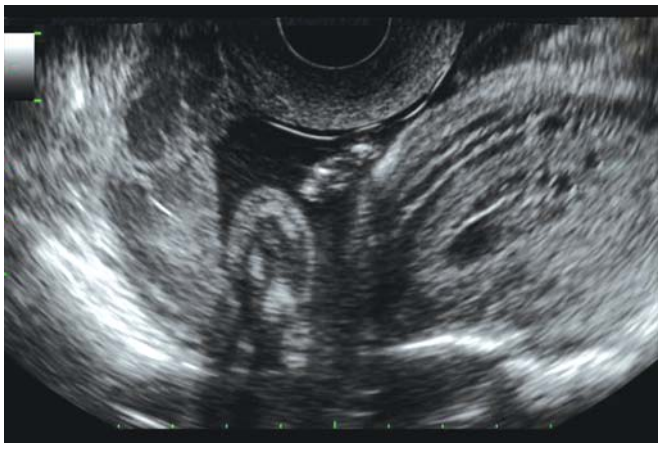


Fig. 31: One fetal death in monochorionic diamniotic twins: The same case after two weeks—signs of periventricular leukomalacia of alive fetus

cordocentesis is not recommended as routine procedure except for suspected hemotologic disease cases.[17]

Ultrasound-guided Therapeutic Interventions in Multiple Pregnancy

Multifetal pregnancy reduction is an out-patient procedure at the 11 to 13th gestation weeks aimed to improve perinatal outcomes of high-order multiples. Essentially, it is an injection of KCl solution in reduced fetus heart provoking cardiac arrest (Fig. 33). Criteria for reduced fetus selection are as follows—ultrasound markers of chromosome abnormality, suspected structural malformations, monochorionic pairs, fetal biometry—CRL is an integral index of potential of successful fetal development as well as various technical details. All these factors shall be taken into account selecting a fetus for the procedure. After multifetal pregnancy reduction from three to four starting fetal number to two fetuses pregnancy loss rate amounts to 5%. It increases to 15% with more fetuses to be reduced. Pregnancy loss rate after multifetal pregnancy reduction increases with increase of pregnancy age.[18]

Malformed fetus selective reduction is the treatment of choice in dichorionic pregnancy. It also implies less of social issues related to decision for reduction procedure and excludes fetus selection necessity prior to the one. In technical sense, it is similar to those described above. In cases of monochorionic pregnancies selective reduction must be done only by reduced fetuses umbilical cord occlusion.

Heterotopic pregnancy interventions. Pregnancy management depends on heterotopic pregnancy location and gestational age.

If extrauterine pregnancy is diagnosed in the first trimester the surgery of choice is laparoscopy. In case of multiple pregnancy with interstitial heterotopic location the most reasonable solution is reduction with KCl injection. If such pregnancy has isthmus-cervical localization such intervention is the method of choice both to save developing uterus pregnancy and preserve patient fertile function.

CONCLUSION

Today ultrasonography is the main method to obtain vital information to manage multiple pregnancy cases which otherwise is almost currently impossible. Multiple pregnancy has a great deal of different complications, so medical professionals should be well-trained and experienced. And it is impossible without everyday clinical work, gaining individual knowledge and skills and being informed on developments and achievements in the best world recognized perinatal centers.

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