

Multiple Pregnancy: Antepartum Death of One Fetus — Risks and Modern Management Approaches

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Abstract Multiple pregnancies occur in 1.5–2.5% of cases, often in families with a history of multiple births, which is associated with the mother's genotype. Assisted reproductive technologies (ART), such as in vitro fertilization and ovulation stimulation, increase the incidence of multiple pregnancies. These pregnancies are associated with a high risk of complications, including preterm birth, low birth weight, and the antenatal death of one fetus. Perinatal mortality in multiple pregnancies is significantly higher compared to singleton pregnancies. Special attention is given to chorionicity, which affects perinatal outcomes. The antenatal death of one fetus causes serious complications for both the surviving fetus and the mother. Successful management of such pregnancies requires a multidisciplinary approach and intensive medical monitoring. Modern diagnostic and treatment methods play a key role in reducing perinatal losses and preserving women's reproductive health.

Keywords Multiple pregnancy, Antenatal death, Pregnancy complications, Preterm birth, Perinatal mortality

Multiple pregnancies occur in 1.5–2.5% of cases, more often in families where one or both parents were born as a result of a multiple pregnancy [1]. The mother's genotype plays a significant role in the predisposition to multiple pregnancies. Interest in this phenomenon has existed since ancient times, but in the last 15-20 years, it has significantly increased due to the rise in frequency, which is associated with the development of assisted reproductive technologies. Modern methods, such as assisted reproductive technologies (ART) and ovulation stimulation, significantly increase the likelihood of multiple pregnancies.

Multiple pregnancies are associated with a high risk of various complications during pregnancy and childbirth. The frequency of cesarean sections, postpartum complications, antenatal losses, and neurological disorders in surviving children is significantly higher compared to singleton pregnancies [9]. Complications include preterm birth, low birth weight, preeclampsia, anemia, and intrauterine growth retardation of the fetuses. These factors significantly increase the risk for both mother and child, necessitating careful medical monitoring and timely intervention.

Patients with multiple pregnancies are considered to be at high risk for perinatal complications. Even with modern medical advancements, perinatal mortality in twin pregnancies is five times higher than in singleton pregnancies, intrauterine fetal death is four times more frequent, and neonatal mortality is six times higher. The incidence of cerebral palsy in twins is 3 to 7 times higher, while in triplets, it is 10 times higher. The level of ante- and intrapartum complications in mothers with

multiple pregnancies exceeds that of patients with singleton pregnancies by 2 to 10 times. These statistics underscore the necessity for intensive medical supervision and specialized care for such patients [15].

Perinatal morbidity and mortality in twins depend on chorionicity, which is the type of placental connection between the twins. Perinatal mortality in monochorionic twins, where both fetuses share a single placenta, is 2.5 times higher than in dichorionic twins, where each fetus has its own placenta. The frequency of preterm births before 32 weeks in monochorionic twins is 10%, compared to 5% in dichorionic twins. The rate of spontaneous abortion in dichorionic twins is 2%, while in monochorionic twins, it is about 10% [17]. These differences are due to the risks associated with shared blood supply in monochorionic twins, which can lead to twin-to-twin transfusion syndrome and other complications.

Multiple pregnancies can be complicated by growth restriction of one or both fetuses, twin-to-twin transfusion syndrome (TTTS), and intrauterine death of one or both fetuses. TTTS occurs in one out of five monozygotic twins with monochorionic placentation [11]. Signs of this syndrome include a difference in fetal weight of more than 20% and varying hemoglobin concentrations between the fetuses. This syndrome develops due to uneven blood supply to the fetuses through connecting vessels in the placenta, leading to an excess of blood in one fetus (the recipient) and a deficiency in the other (the donor) [3]. Treatment may involve laser coagulation of the connecting placental vessels to restore the balance of blood supply.

The most common factor associated with ante- and neonatal mortality and morbidity in twin pregnancies is low

birth weight, which in most cases is due to preterm birth. Preterm birth leads to underdevelopment of the baby's organs and systems, increasing the risk of various complications. Various hypotheses explain the threat of pregnancy termination in multiple pregnancies, including overstretching of the uterine muscle fibers and infection of the amniotic membranes, leading to preterm labor [1].

Systematic reviews demonstrate the high effectiveness of antenatal screening and treatment of lower genital tract infections in reducing the incidence of preterm births and associated complications. Neurological complications are a significant issue in multiple pregnancies, especially in preterm infants and those with growth restriction. These complications include cerebral palsy, delayed psychomotor development, and other neurological disorders that can substantially impact the child's quality of life [14].

Preterm birth is the leading cause of neonatal mortality and disability in multiple pregnancies. The frequency of preterm births in economically developed countries varies from 6% to 12%, with approximately 40% occurring before the 34th week and 20% before the 32nd week. Preterm births account for more than 50% of all perinatal losses and complications. Premature infants are at a higher risk of developing respiratory, cardiovascular, and neurological problems, requiring specialized care in neonatal intensive care units [10].

Antenatal death of one of the fetuses is a specific complication of multiple pregnancies, occurring in 6% of cases. The frequency depends on the degree of multiplicity: it is twice as high in triplets as in twins and is even more pronounced in relation to chorionicity. Etiological factors of fetal death in multiple pregnancies include discordant conditions affecting one fetus and complications impacting both fetuses. The death of one fetus can cause significant stress for the parents, requiring psychological support and counseling [2].

The phenomenon of "vanishing twin syndrome" describes an embryo that predominantly dies before 10 weeks of gestation and is subsequently absorbed or miscarried. In dichorionic twins, this does not affect the development of the surviving fetus, whereas in monochorionic twins, it is associated with the risk of growth restriction and cerebral palsy. Studies show that about 20-30% of multiple pregnancies may begin as multiples but result in the birth of a single child due to the "vanishing twin" phenomenon [2].

The pathogenetic mechanisms affecting the surviving fetus after the intrauterine death of a co-twin include blood circulation through placental anastomoses, hypotension, hypoperfusion, anemia, coagulopathy, and ischemic organ damage. The impact of intrauterine death of one fetus on perinatal outcomes depends on chorionicity: neurological complications occur in 18% of cases in monochorionic twins and in 1% in dichorionic twins, while preterm birth occurs in 68% and 57% of cases, respectively [2].

The three main forms of brain injury in the surviving fetus in monochorionic twins include hypoxic-ischemic injuries, hemorrhagic injuries, and a combination of congenital malformations of the nervous system with hypoxic-ischemic

and hemorrhagic lesions. Extracerebral injuries include small bowel atresia, hydrothorax, and other pathologies [4].

In the case of a terminal condition in one fetus of a monochorionic twin pregnancy, selective feticide is recommended to prevent complications for the surviving fetus. If reduction is not possible, the management strategy is similar to that used in the intrauterine death of one fetus [13].

To diagnose anemia in the surviving fetus, Doppler ultrasonography is used to determine the peak systolic velocity in the middle cerebral artery. Medical care for the intrauterine death of one fetus should be provided in tertiary care centers. It is crucial to promptly identify and treat complications in the surviving fetus to minimize the risk of neurological and other disorders [16].

If one fetus dies antenatally in the early second trimester, parents should be counseled on the possibility of pregnancy termination. At 25-27 weeks of gestation, thorough fetal assessment is necessary, and at 28-34 weeks, pregnancy should be prolonged if there are no signs of fetal distress. An absolute indication for delivery is the intrauterine death of one fetus at 34 or more weeks of gestation [2].

The frequency of preterm births does not decrease, and there is no effective method of prevention in twin pregnancies. Diagnosing preterm labor in multiple pregnancies is challenging but can be clarified using transvaginal ultrasound and fetal fibronectin testing in the cervicovaginal secretions [5].

Systematic reviews demonstrate the high effectiveness of antenatal corticosteroid therapy in reducing morbidity and mortality in infants. It is crucial to timely transport pregnant women at high risk of preterm labor to a perinatal center. These measures help improve the survival and health outcomes of preterm infants [5].

Tocolytic therapy, including magnesium sulfate, is widely used in obstetric practice. Magnesium sulfate has anticonvulsant properties and a neuroprotective effect, reducing the risk of cerebral palsy in preterm newborns. Calcium channel blockers and prostaglandin synthesis inhibitors are also used, although they may cause undesirable side effects [6].

Progesterone is used for the prevention of preterm labor, particularly in singleton pregnancies, but its effectiveness in twin pregnancies has not been proven. β -mimetics are also used in the protocols of tocolytic therapy for preterm labor. These medications help prolong pregnancy, which can significantly improve outcomes for newborns [7,8].

The administration of antibiotics in cases of preterm premature rupture of membranes (PPROM) reduces the incidence of chorioamnionitis and neonatal morbidity. A systematic review of 22 randomized controlled trials showed that the use of antibiotics in cases of PPRM and preterm pregnancy significantly reduces the incidence of chorioamnionitis and the number of infants born within 48 hours after membrane rupture. Additionally, the use of antibiotics in this clinical situation decreases the frequency of neonatal infections, the need for surfactants, oxygen therapy in newborns, and the occurrence of pathological

findings on neurosonography [12].

Thus, patients with multiple pregnancies are at high risk for maternal and perinatal complications. This is directly related to the fact that, evolutionarily, a woman's body is adapted to carry a single fetus. The key to the successful management of multiple pregnancies and the care of newborns lies in the continuity of all obstetric and gynecological departments and the neonatal units within the maternity facility. Further research on this issue should aim at reducing perinatal losses and preserving the reproductive health of women.

Effective management of multiple pregnancies requires a multidisciplinary approach involving obstetricians-gynecologists, neonatologists, anesthesiologists, and other specialists. Continuous monitoring of the mother's and fetuses' condition, timely detection and treatment of complications, and psychological support for the parents are essential. Modern diagnostic and treatment methods, such as Doppler ultrasound, ultrasound imaging, and magnetic resonance imaging, play a key role in ensuring favorable outcomes for both mother and children.

In addition to medical aspects, social support for families with multiple pregnancies is also important. Informing parents about potential risks and complications, as well as methods of prevention, can help reduce anxiety levels and improve the overall health of the mother and children.

Prospects for the development in the study of multiple pregnancies include further research into the genetic factors influencing the development of multiple pregnancies, the improvement of methods for diagnosing and treating complications, and the development of new strategies for preventing preterm labor. The integration of innovative technologies and approaches into medical practice will significantly enhance the quality of healthcare and improve perinatal outcomes for mothers and their children.

In conclusion, multiple pregnancies are a complex and multifaceted phenomenon requiring careful and comprehensive management and treatment. Successful gestation and delivery of multiple pregnancies are possible through close collaboration among medical professionals, the use of modern diagnostic and therapeutic methods, and the provision of social and psychological support for families.

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