Review Article

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Neonatal Outcome and Management in Twin Gestation

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Abstract

The incidence of multiple pregnancy and delivery has increased dramatically over the past 10–15 years in many developed countries of the world. Data for England and Wales show that between 1980 and 1993 the twin maternity rate increased by <"25% and the triplet and higher order maternity rate more than doubled. Similar trends have been reported from developing countries. The majority of these increases have been linked to the use of ovarian stimulants and assisted reproduction techniques, and multiple pregnancy must be considered to be one of the most important adverse outcomes in current methods of infertility treatment. Obstetric complications associated with multiple pregnancy include prenatal screening problems and increased incidence of pregnancy-induced hypertension, antepartum haemorrhage, preterm labour and assisted or surgical delivery. Neonatal problems include low birthweight and increased prevalence of congenital malformations. Compared with singletons, neonatal mortality is seven times higher in twins and >20 times higher in triplets and higher order births. Survivors also suffer higher rates of cerebral palsy and other neurological impairments.

This article reviews neonatal complications and management of twins.

Keywords: Twins; TTTS; TRAP; Thoracopagus.

Introduction

The incidence of multiple pregnancies has increased enormously over the last three decades due to increases in ovulation induction, *in vitro* fertilization (IVF) as well as childbearing at older ages. Multiple gestations are high risk pregnancies that may be complicated by maternal and neonatal morbidity and high neonatal and infant mortality. The offspring of multiple gestations may carry additional risk for long-term consequences of perinatal complications, including cerebral palsy and learning disabilities.[1] It seems that marked improvement of neonatal care as well as thorough obstetric follow-up could positively influence the outcome of multiple pregnancies.

Objective

To review literature regarding the neonatal outcomesfollowing twin delivery.

Data Sources

Searches were conducted in PubMed, Medline, Embase, Cochrane library and reference lists as well as textbooks and manuals of neonatal medicine.

Incidence

The twin birth rate in 2006 was 32.1 per 1,000 live births and had been stable for the previous 2 years.

The rate of MZ twinning has remained relatively constant (3.5 per 1,000 births). The

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rate of DZ twinning is approximately 1 in 100 births. This rate is influ-enced by several factors such as ethnicity (1 in 500 Asians, 1 in 125 in whites, and as high as 1 in 20 in African populations) and maternal age.[2]

Causative Factors

Two main factors account for the increase in multiple births over the last 2 decades: (i) increased use of fertility-enhancing therapies, includ-ing assisted reproductive technologies (ARTs) such as *in vitro* fertilization (IVF), and non-ART therapies such as ovulation-inducing drugs and artificial insemina-tion, and (ii) older maternal age at childbearing (peak at 35-39 years), which is associated with an increase in multiples.[2]

The incidence of dizygotic twinning increases with a family history of twins, maternal age (peak at 35-39 years), previous twin gestation, increasing parity, maternal height, fecundity, social class, frequency of coitus, and exposure to exogenous gonadotropins (20-40% incidence) and clomiphene (6-8% incidence).

Zygosity

MZ pregnancies result from the splitting of a single egg between day 0 and day 14 postfertilization. The type of placenta that forms depends on the day of embryo splitting.At day 14 and thereafter, the primitive streak begins to form, and late splitting of the embryo at this time results in conjoined twins.[3]

DZ or multizygous pregnancies result when more than one dominant fol-licle has matured during the same menstrual cycle and multiple ovulations occur.

Maternal Complications

These include Gestational diabetes, Spontaneous abortion, Incompetent cervix, Placental abruption, Preterm premature rupture of membranes, Pregnancy-induced hypertension (PIH) and preeclampsia and Cesarean delivery.[2]

Fetal and Neonatal Complications

Neonates born to multiple fetal pregnancies may present unique personnel requirements at delivery and during hospitalization. Delivery room management requires adequate personnel skilled in neonatal resuscitation.

1) Prematurity and Low Birth Weight: The average duration of gestation is shorter in multifetal pregnancies and further shortens as the number of fetuses increases. The mean gestational age at birth is 36, 33, and 29 and one-half weeks, respectively, for twins, triplets, and quadruplets. In developed countries, the incidence of preterm birth in twins was 60.4% in 2006, compared with 11.1% in singletons. Although most of this increased incidence is due to mild prematurity, multifetal pregnancy increases the risk of severe prematurity and very low birth weight (VLBW). The likelihood of a birth weight <1,500 g is 8 and 33 times greater in twins and triplets or higher order multiples, respectively, compared with singletons. In two multicenter surveys, multiples occurred in 21% to 24% of births <1,500 g and in 30% of births < 1,000 g.[4]

2) Intrauterine growth restriction (IUGR): Fetal growth is independent of the number of fetuses until approximately 30 weeks' gestation, after which growth of multiples gradually falls off compared with singletons. IUGR is defined as an estimated fetal weight (EFW) less than either the third percentile for gestational age or an EFW < 10th percentile for gestational age with evidence of fetal com-promise. The mechanisms are likely uterine crowding, limitation of placental per-fusion, anomalous umbilical cord insertion, infection, fetal anomalies, maternal complications (e.g., maternal hypertension), and monochorionicity. Monochori- onic twins are more likely than dichorionic twins to be IUGR and have higher perinatal mortality.[2]

3) Fetal growth discordance is typically

defined as an intrapair difference in birth weight of more than 20% of the larger twin's weight. It can also be categorized as mild (<15%), moderate (15%-30%), or severe (>30%). Risk factors for discordant growth include monochorionic placentation as-sociated with velamentous cord insertion, placental dysfunction, preeclamp-sia, antepartum bleeding, twin-to-twin transfusion syndrome (TTTS), fetal infection, and fetal structural and chromosomal abnormalities. The smaller twin has an increased risk of fetal demise, perinatal death, and preterm birth. Five percent to 15% of twins and 30% of triplets have fetal growth discor-dance that is associated with a sixfold increase in perinatal morbidity and mortality.[2,5]

4) Intrauterine fetal demise (IUFD) refers to fetal demise after 20 weeks' gesta-tion but before delivery and is confirmed by ultrasonographic evidence of absent fetal cardiac activity. The death of one twin, which occurs in 9% of multiple pregnancies, is less common in the second and third trimesters. The risk of IUFD is four to six times greater in MZ pregnancies. Since almost all MZ twins have placental vascular connections with resulting shared circulations, there is a significant risk (20%-40%) of neurologic injury (multicysticencephaloma- lacia) in the surviving co-twin as a result of associated severe hypotension or thromboembolic events upon death of the co-twin. Because their circulation is not shared, the death of one DZ twin usually has minimal adverse effect on the surviving co-twin. In this case, the co-twin is either completely resorbed if death occurs in the first trimester or is compressed between the amniotic sac of its co-twin and the uterine wall (*fetuspapyraceous).* Other complications involv-ing the surviving co-twin include antepartum stillbirth, preterm birth, placental abruption, and chorioamnionitis.[2,5,6]

5) Congenital malformations occur in approximately 6% of twin pregnancies, or 3% of individual twins. The risk in MZ twins is approximately 2.5-fold greater than in DZ twins or singletons.

Structural defects specific to MZ twins include:

a) early malformations that share a common origin with the twinning process,

b) vascular disruption syndromes, and

c) deformations.[2]

a) Early structural defects include the following:[2,6]

- Caudal malformations (sirenomelia, sacrococcygealteratoma)
- Urologic malformations (cloacal or bladder exstrophy)
- The VATER spectrum (vertebral anomalies, anal atresia, tracheoesophageal fistula, renal agenesis, cardiac defects)
- Neural tube defects (anencephaly, encephalocele, or holoprosencephaly)
- Defects of laterality (situsinversus, polysplenia, or asplenia)

b) Vascular disruption syndromes may occur early or late in gestation.[6]

The presence of large anastomoses between two embryos early in develop-ment may cause unequal arterial perfusion resulting in acardia. Profound malformations can result ranging from complete amorphism to severe upper body abnormalities such as anencephaly, holoprosencephaly, rudimentary facial features and limbs, and absent thoracic or abdominal organs. The co-twin is usually well formed. Acar-dia is rare, occurring in 1% monoamniotic twin pregnancies and affecting 1 in 35,000 to 150,000 births. Resulting mal-formations include cutis aplasia, limb interruption, intestinal atresia, gastros- chisis, anorchia or gonadal dysgenesis, hemifacialmicrosomia, Goldenhar syndrome (facio-auriculo-

vertebral defects), or Poland sequence. Cranial ab-normalities include porencephalic cysts, hydranencephaly, microcephaly, and hydrocephalus.

c) Deformations such as clubfoot, dislocated hips, and cranial synostosis are more frequent in multiple pregnancies as a result of overcrowding of the intra-uterine environment.

6) Chromosomal anomalies occur at a higher frequency in offspring of multiple gestations. Advanced maternal agecontributes to the increased risk in chromo-somal anomalies. The risk in MZ twins is equivalent to that of a singleton. The risk in DZ twins is independent for each fetus, so the risk of chromosomal abnor-mality in at least one DZ twin is twice that of a singleton fetus.[7]

7) Conjoined twins[6,9] result when incomplete embryonic division occurs late, after day 14 postconception. The most common sites of fusion are the chest and/or abdomen. Survival is rare when there is cardiac or cerebral fusion. Serial ultrasonog-raphy can define the fetal anatomy and help determine management options. Poly-hydramnios can affect as many as 50% of cases of conjoined twins and may require amnioreduction.

Conjoined twins are connected at identical points and are classified according to site of union; as follows:

Thoracopagus – Joined at chest (40%)

Fig 1: Twin to Twin Transfusion Syndrome (TTTS)

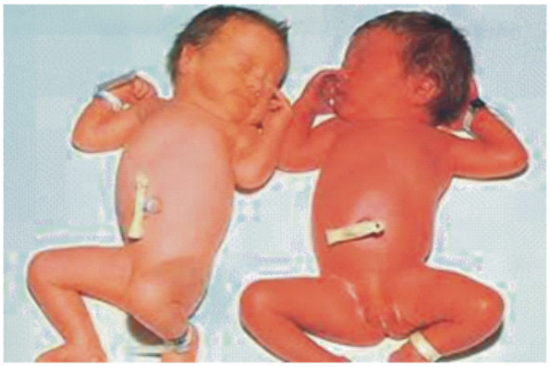
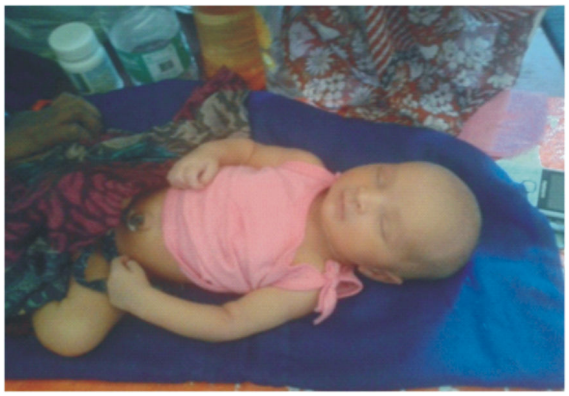
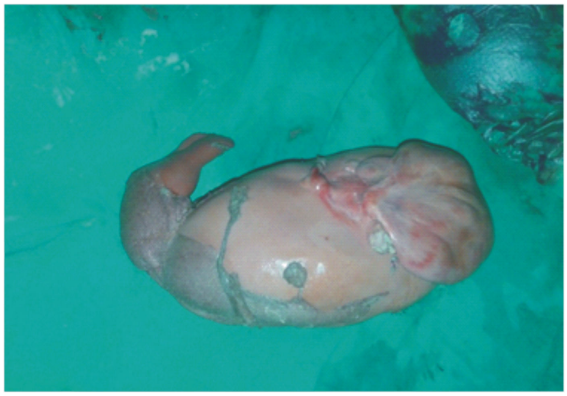


Fig 2: TRAP (Twin reversed arterial perfusion) Sequence





Xiphopagus/omphalopagus – Joined at abdomen (34%)

Pygopagus – Joined at buttocks (18%)

Ischiopagus – Joined at ischium (6%)

Craniopagus – Joined at head (2%)

Fetal Lung Maturity in Multiple Gestation

At this point, consensus is lacking on whether pulmonary mat-uration differs between singleton and multiple pregnancies. If age-specific risks of develop-ing respiratory distress syndrome are similar for twins and for singletons, new guidelines will be needed to avoid false-positive prediction of adequate lung maturity in twins. However, antenatal steroids must be used if the delivery is likely to be before 34 wks.[6]

Twin-to-Twin Transfusion Syndrome[6,9,10]

TTTS is a complication of monochorionic pregnancies character-ized by an imbalance

in the blood flow across a shared placenta of two fetuses. The net effect of this imbalance in fetal support is marked developmental discrepancy, with a large, hyperperfused recipient twin and a small, hypoperfused and anemic donor twin. If the condition goes untreated, the prognosis is poor, with a 60% to 100% mortality rate for both twins. When one twin dies in utero, the surviving twin is at risk for severe neurologic dam-age. The true incidence of TTTS is unknown, because many of these pregnancies result in early loss. TTTS results from absence of the superficial anastomoses that maintain balanced blood flow.

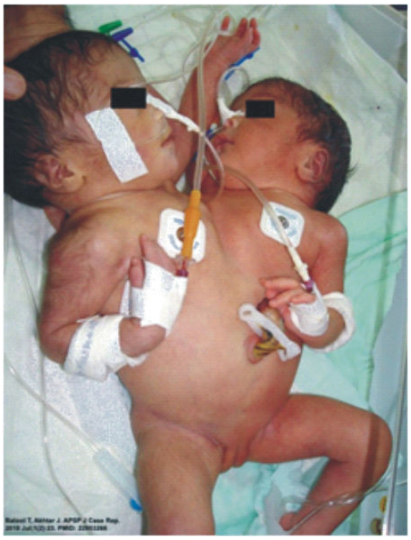
Antenatal Diagnosis of TTTS is made by ultrasound imaging. The four requirements for the diagnosis of TTTS are (1) the presence of a single placenta, (2) same-gender fetuses, (3) weight discor-dance of greater than 20%, and (4) significant amniotic fluid dis-cordance, with the recipient twin may exhibit signs of heart failure and hydrops.

Weight and hematologic discordances are no longer consid-ered diagnostic of TTTS.

The differential diagnosis for TTTS includes abnormal cord insertion or uteroplacental insufficiency with poor fetal growth and decreased urine output in one twin and fetal anomalies, such as bladder obstruction and aneuploidy management option for TTTS is serial reduction amniocen-tesis. Antenatal corticosteroids should be administered to the mother if delivery is anticipated between 24 and 34 weeks. If either fetus shows compromise between 32 to 34 weeks, immediate delivery should be considered.

Neonatal management may include resuscitation at birth and need for contin-ued ventilatory and cardiovascular support, rapid establishment of intravascular access for volume expansion to treat hypotension, correction of hypoglycemia, red blood cell transfusion to treat anemia, and partial exchange transfusion in the recipient to treat significant polycythemia. Neuroimaging is performed to detect central nervous system (CNS) injury.

Fig 3: Conjoined twins (Thoracopagus)



Persistent pulmonary hypertension of the newborn (PPHN).TTTS is as-sociated with a greater frequency (up to 3%) of PPHN compared to mono- chorionic twins without TTTS. The association between PPHN and TTTS may result from increased preload, volume overload, polycythemia, increased pulmonary vascular resistance, and increased afterload due to vasoactive sub-stances in the recipient twin. In contrast, the donor twin may also be suscep-tible due to the presence of IUGR and lower levels of specific amino acids, such as arginine, which, as a nitric oxide precursor, plays a role in decreasing pulmonary vascular resistance after birth.[2]

Twin Reversed Arterial Perfusion Syndrome[2,6]

TRAP, also known as acardia, is defined by the absence of a nor-mally functioning heart in one fetus of a multiple pregnancy.The incidence is estimated to be 1% of monozygotic twin pregnan-cies. Reversal of blood flow in the umbilical artery of the recipient twin is character-istic, and deoxygenated blood is brought from the pump twin to the acardiac twin. As a result, the gestation includes a normal twin and an amorphous twin.

The goal of management is to optimize the outcome for the/normal twin. Poor prognosis has been associated with polyhydramnios and

congestive heart failure in the pump twin.

Neonatal Implications and Management[2,3,9]

Site of Delivery: When a complicated twin gestation has been identified, delivery should ideally be conducted at a high-risk perinatal center with two experienced pediatric delivery teams in attendance.

Physical Examination: Infants should be examined for evidence of intrauterine growth retardation, congenital anomalies, and twin-twin transfusion syndrome. Central hematocrits should be obtained in both infants to look for anemia or polycythemia. When one of the infants has a congenital anomaly, the normal twin is at increased risk for complications of pregnancy and growth retardation. In particular, death of one fetus puts the others at risk for fetal disseminated intravascular coagulation. Resulting cystic encephalomalacia is estimated to occur in 12% of monochorionic twin gestations.

Complications in Newborn Period: The second-born twin is 2-4 times as likely to develop respiratory distress syndrome probably secondary to perinatal stress; however, the first-born twin may be at risk for necrotizing enterocolitis .

Cobedding of Multiples: Coincident with the rise in multiple births has been an interest in cobedding of multiples. Among other criteria, eligible multiples need to be free of infection, have stable temperature in an open crib, have no indwelling catheters, and be on room air or nasal cannula.hospital cost is certainely reduced.[11]

Feeding: Most of the twins can be successfully breastfed. However, if there is insufficient milk, appropriate formula feeding may be used for optimal growth.

Outcomes{1,2,9,12,13]

Neonatal Mortality: Twin birth is associated with an increased risk of neonatal mor-tality compared to singleton births at all gestational ages; the perinatal mortality rate is increased further in second-born twins compared to first-born twins (26.1 vs. 20.3 per 1,000 live births). The mortality increases threefold and fourfold for triplet and quadruplet births, respectively. As with singleton births, mortality is inversely proportional to gestational age. In addition, the perinatal mortality rate in twin pregnancies peaks again with advancing gestational age, particularly after 37 weeks' gestation; delivery at 37 to 38 weeks is considered optimal timing of twin delivery. Prematurity and low birth weight are the predominating factors that increase the rates of mortality and morbidity for multiple births.

Morbidity

Prematurity and growth restriction are associated with an increased risk of morbidities such as bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, and intraventricularhemorrhage. These morbidities need early diagnosis and management for better outcome.

Catch-up Growth: In monozygotic twins, birth weight differences may be as much as 20%, but the lighter twin has a remarkable ability to make up intrauterine growth deficits. However, if the birth weight of the lighter twin is less than the 10th percentile, the prognosis is guarded. With such marked discordance, the undersized twin often continues to be inferior in growth and intelligence into adult life.

Long-term morbidity such as CP and other neurologic handicaps affects more twins and multiples than singletons. The risk of CP in multiples compared with singleton gestations is increased from fivefold to tenfold. Twins account for 5% to 10% of all cases of CP in the United States. The prevalence of CP in twins is 7.4%, compared with 1% in singletons. The higher prevalence of CP among twins compared to singleton births is due to a greater frequency of prematurity and low birth weight in twins, as well as a higher prevalence of CP among larger twin pairs. Death of a co-twin is considered an independent risk factor for CP in the surviving twin. Twins have a greater

risk of learning disabilities even after controlling for CP and low birth weight.

Acquired Illnesses: Illness in one twin increases the risk of illness in the other. Epilepsy has an 85% concordance rate in identical twins. With acute lymphocytic leukemia or juvenile diabetes mellitus of one twin, the incidence in the other twin is 20% and 50%, respectively.

Impact of Assisted Reproductive Technology on Outcomes[14]

There have been multiple reports of increased adverse maternal and perinatal outcomes associated with ART. However, the extent to which the disproportionate increased frequency of multiple births (30% twin births with ART vs. 1.5% with non-ART deliveries) following ART contribute to this risk requires further study.

Economic Impact: Hospital stays for mothers and babies are typically longer for multiple gestations. One study estimated that, compared with singletons, average hospital costs were three and six times higher for twins and triplets, respectively; the total family costs were four and 11 times higher, respectively.15

Social and Family Impact: Caring for twins or higher order multiples contributes to increased marital strain, financial stress, parental anxiety, and depression and has a greater influence on the professional and social life of mothers of these in-fants, particularly first-time mothers, compared with mothers of singletons. Multiples are more likely to have medical complications (i.e., prematurity, con-genital defects, IUGR) that result in prolonged hospital stays that contribute fur-ther to a family's emotional and financial stress.[2]

Key Messages

- The incidence of twins/multiples has increased over last decade.
- Twins develop various complications during intrapartum and neonatal period.
- Most common problems are prematurity and congenital malformations.
- Twins may develop long-term neurodevelopmental and behavioural problems.

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