COMPLICAZIONI MATERNE E FETALI NELLA GRAVIDANZA GEMELLARE





Incidenza delle gravidanze gemellari

Twins constitute 2%-4% of all births, and the rate of twining has increased by 76% between 1980 and 2009.





Twinning rate in selected European countries (1970-2003)

Per 1,000 deliveries



Source: Pison & D'Addato, 2006.



Dizygotic twins

- Most common represents 2/3 of cases.
- Fertilization of more than one egg by more than one sperm.
- Non identical ,may be of different sex.
- Two chorion and two amnion.
- Placenta may be separate or fused





Dizygotic twins

two eggs fertilized by two different sperms - genetically different



Dichorionic Diamniotic: separate/fused placentas and membranes

Benirschke K, Obstet Gynecol 1961 Benirschke K, N Engl J Med 1973



- Induction of ovulation, 10% with clomide and 30% with gonadotrophins.
- Increase in maternal age ? Due to increase gonadotrophins production.
- Increases with parity.
- Heredity usually on maternal side.
- Race; Nigeria 1:22 North America 1:90.



Monozygotic twins

- Constant incidence of 1:250 births.
- Not affected by heredity.
- Not related to induction of ovulation.
- Constitutes 1/3 of twins.





Separation in Monozygotic twins

one fertilized egg - genetically identical



Benirschke K, Obstet Gynecol 1961 Benirschke K, N Engl J Med 1973



Maternal physiological

adaptation to twin pregnancy

- Cardiovascular
- Hematologic
- Gastrointestinal and hepatic
- Urinary tract
- Metabolic



Cardiovascular adaptation

Differences between singletons and twin gestations appear as early as the first trimester

In a study comparing 119 twin pregnancies with 128 singleton controls maternal ventricular function was assessed by echocardiography

Twin gestation was characterised by

Increased cardiac output secondary to:
a) higher stroke volume
b) Faster heart rate



Cardiovascular adaptation

- Increase in left atrial diameter
- Increase in left ventricular end- diastolic diameter

Refrecting therefore an increase in preload for twin gestations

These cardiac adaptations are not significant for women with intact baseline cardiovascular function, however those with cardiovascular or congenital heart disease may reach the limit of their adaptive capabilities earlier with a twin gestation



Hematologic adaptations

- Blood volume in a twin pregnancy increases 50-70% by 20 weeks compared with only 20% with a singleton pregnancy
- Only a 25% increase in erythrocytes with therefore a hemodiluitional anemia resulting in : decreased concentration of hemoglobin, albumin, water soluble vitamins
- Higher rates of iron- defficiency anemia compared with singleton gestations



Gastrointestinal and hepatic

Pregnancy nausea and vomiting is seen in 50% of multiple pregnancies

The incidence of obsteric cholestasis in women genetically susceptible to intrahepatic cholestasis is nearly <u>twice</u> that of sigleton pregnancies

9-25% of cases of acute fatty liver are seen in twin pregnancies and early diagnosis and delivery reduces maternal mortality



Urinary tract

Ureteral dilatation with decreased peristalsis from high levels of progesterone and compression of the ureters by the over distended uterus can lead to stasis and urinary tract infections more often in twin pregnancies than in sigleton pregnancies

The incidence of pyelonephritis does not seem to be increased



Twin gestations have higher metabolic rates than singleton pregnancies with maternal resting expenditure increased by 10%

Increase in metabolic rates results in a 40% increase in caloric requirements



Optimal Nutrition for Improved Twin Pregnancy Outcome

William Goodnight, MD, MSCR, and Roger Newman, MD, for the Society of Maternal-Fetal Medicine (Obstet Gynecol 2009;114:1121-34)

- "The goals for optimization of maternal nutrition in multiple gestations include: •
 - Optimizing fetal growth and development
 - Reducing incidence of obstetrics complications
 - Increasing gestational age at delivery" .

1- Adeguato apporto calorico correlato al BMI pregravidico

	Underweight	Normal Weight	Overweight	Obese
Calories (kcal)	4,000	3,000-3,500	3,250	2,700-3,000
Protein (g)*	200	175	163	150
Carbohydrate (g)*	400	350	325	300
Fat (g)†	178	156	144	133
* # June 1/m				

Table 1. Suggested Daily Diet Composition for Twin Gestation by Maternal Prepregnancy Body Mass Index¹⁴

4 Kcal/g.

 † 9 kcal/g.



Complications of multiple pregnancies

Maternal Complications	Uteroplacental Complications	Fetal Complications
 Spontaneous abortion Anemia Hyperemesis gravidarum Gestational diabetes Preterm labor and birth Pregnancy-induced hypertension/ preeclampsia Cesarean delivery 	 Placenta previa Placental abruption Preterm premature rupture of membranes Cord entanglement Postpartum hemorrhage 	 Fetal growth discordance Intrauterine growth restriction Intrauterine fetal demise of one or both twins Congenital anomalies Malpresentation Twin-to-twin transfusion syndrome Twin reversed arterial perfusion (TRAP) syndrome



Antepartum morbidity

Hypertensive disorders / preeclampsia

Incidence: singletons 5-10% twins 10-20%

Preeclampsia is defined as gestation- related hypertension combined with proteinuria

The risk may be directly correlated with the number of fetuses, as higher order multiples have increasing risks of developing preeclampsia perharps in part secondary to the larger placental volume

Additionally, women who become pregnant with multiple gestations through assisted reproductive technologies have a 2-fold risk of preeclampsia compared with spontaneous twin conceptions



Hypertensive disorders of pregnancy

Compared to singleton pregnancies, women with twin gestations have higher rates of gestational hypertension (RR 2.04; 95% Cl 1.60–2.59) and pre-eclampsia (RR 2.62; 95% Cl 2.03–3.38).¹⁸ In addition, the onset of pre-eclampsia is often earlier and the severity greater. When gestational hypertension develops there is a significantly higher rate of delivery prior to 37 weeks gestation (51.1% versus 5.9%), delivery prior to 35 weeks gestation (18.2% versus 1.6%) and the birth of small-for-gestational-age infants (14.8% versus 7.0%).¹⁸ Significantly higher rates of preterm delivery and abruptio placenta are also noted with pre-eclampsia in twin pregnancy (66.7% versus 19.6% for delivery at <37 weeks gestation, 34.5% versus 6.3% for delivery at <35 weeks gestation, 4.7% versus 0.7% for abruptio placenta).¹⁸

Women with twin pregnancy and pre-eclampsia are more susceptible to volume overload and pulmonary oedema due to the combination of afterload caused by vasospasm and increased preload caused by baseline increase in plasma volume. The management of pre-eclampsia is twin pregnancy is similar to that of singleton pregnancy but must include extra precautions to control blood pressure and avoid excessive intravenous fluid administration, as well as closer monitoring for evidence of lifethreatening complications.



Hypertensive disorders / preeclampsia

There is an increased rate (x4) of development of Hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome for women carrying a twin pregnancy compared with a singleton

One retrospective analysis indicated that dichorionic twins were nearly twice as likely to develop preeclampsia compared with monochorionic twins



Advise women with twin and triplet pregnancies that they should take 75 mg of aspirin daily from 12 weeks until the birth of the babies if they have one or more of the following risk factors for hypertension:

- •first pregnancy
- age 40 years or older
- •pregnancy interval of more than 10 years
- •BMI of 35 kg/m2 or more at first visit
- •family history of pre-eclampsia.



- Gestational diabetes results from relative insulin insufficiency secondary to the diabetogenic effect of placental hormones (human placental lactogen, progesterone and cortisol).
- The larger placental mass of multiple pregnancy increases the amount of these placental hormones and therefore, theoretically the risk of developing gestational diabetes.

There is no evidence of increase in gestational diabetes in twins compared to singletons

Buhling KJ Arch Gyn Obs 2003



Twin pregnacies have increased risk of 3 rd trimester bleeding from

- Placenta previa (40% increased risk compared to singletons)
- Placental abruption: may occur from an overdistended uterus as well as from sudden decompression with rupture of membranes

Complicanze fetali

4 I P

- Gravidanza monoamniotica
- Conjoined twins
- Twins discordant for anomaly
- TRAP syndrome
- TTTS
- Morte endouterina di 1 gemello
- PPROM di 1 sacco amniotico
- Parto pretermine di 1 gemello



- Parto pretermine
- IUGR



Unrestricted fetal movement and absence of a dividing membrane



Single placenta and same sex twins
Close approximation of the cord insertions
Entanglement of the cords
Normal and identical amniotic fluid volume around both fetuses

Aprile 2008





1/35.000 pregnancies

1% of monochorionic twins (di- and monoamniotic)

Superficial anastomosis Acardiac twin Pump twin



Natural History



A-A and V-V anastomoses within the placenta allow retrograde perfusion of the acardiac twin by blood coming from the normal twin

mortality of the normal twin > 50% (high-output cardiac failure) preterm delivery (subsequent to polyhydramnios)



Conjoined twins

1:30.000 to 1:100.000 births Divison of embrionic disk > 13 days after fertilization



75% are stillborn or die within 24 hours

Barth RA et al, Radiology 1990; 177:201-207





Conjoined twins

56% Thoracopagus Omfalopagus Thoraco-omfalopagus



75% of thoracopagus twins have extensively conjoined hearts that preclude successful surgical separation

Barth RA et al, Radiology 1990; 177:201-207



Preterm labour

Preterm births in 2006: twin vs singleton



BW, birthweight; *Cl*, confidence interval; *Del*, delivery; *OR*, odds ratio. Data derived, with permission, from Martin et al.²

Chauhan. Twins: prevalence, problems, and preterm births. Am J Obstet Gynecol 2010.

Twins are five times more likely to be born preterm compared with singletons, and eight times more likely to be born <32 weeks.

Delivery before 32 weeks is twice as common in MC twins (9.2%) compared to DC twins (5.5%).



Preterm labour

Preterm delivery caused

•spontaneous preterm labour

preterm prelabour
 rupture of membranes

•iatrogenic factors



Identificazione delle gravidanze a rischio per parto pretermine raccomandazioni SIEOG 2011



- a. indipendentemente dalla corionicità, la gravidanza gemellare presenta un rischio di parto pretermine spontaneo o PPROM 5 volte maggiore rispetto alla gravidanza singola, e, complessivamente, i gemelli rappresentano il 15% di tutti i neonati prematuri;
- b. la determinazione della lunghezza della cervice uterina mediante ecografia transvaginale dovrebbe essere eseguita tra 20 e 24 settimane;
- c. in pazienti asintomatiche la presenza di una cervice < 20 mm tra 20 e 24 settimane è il dato che correla maggiormente con il parto pretermine <32 e < 34 settimane (likelihood ratio + 10)
- d. non vi sono dati che confermino il ruolo della fibronectina o della IGF BP nella identificazione delle gravidanze gemellari a rischio di parto pretermine
- e. non è stato dimostrato alcun effetto protettivo del progesterone nella prevenzione del parto pretermine nella gravidanza gemellare
- f. analogamente, non vi sono studi che confermino la utilità del cerchiaggio nelle gravidanze gemellari



Fetal growth restriction

Twin pregnancies have **10 fold** risk of delivering growth-restricted babies compared to singletons

High frequency of growth restriction complicated by premature deliveries contributes significantly to the high perinatal mortality and morbidity in twin pregnancies

Pathological discordant growth is defined as discordant fetal weight > 30% difference



Fetal growth restriction

A study demonstrated that the chance of having atleast one growth restricted twin was

- 34% for monochorionic twins
- 23% in dichorionic twins

Chance of both twins having growth restriction was X4 in MC pregnancies

Sebire NJ Obs & Gyn 1998



Fetal growth restriction



Single intrauterine demise

- •2-6% of twins pregnancies
- •Up to 25% in MC twin pregnancy
- Perinatal morbidity and mortality of the surviving co-twin
- 19% perinatal death
- 24% having serious long term sequelae



Treatment options

•No optimal management

•Prompt delivery -latrogenic prematurity risks

•Conservative treatment -Subsequent handicaps

•Intrauterine interventions



Morbidità e mortalità neonatale

Characteristic	Twins	Triplets	Quadruplets
Average birth weight	2347 gm	1687 gm	1309 gm
Average gestational age at delivery	35.3 wks	32.2 wks	29.9 wks
Percentage with growth restriction	14-25	50-60	50-60
Percentage requiring admission to NICU	25	75	100
Average length of stay in NICU	18 days	30 days	58 days
Percentage with major handicap	-	20	50
Risk of cerebral palsy	4 x more than singletons	17x more than singletons	-
Risk of death by 1 year	7x higher than singletons	20 x higher than singletons	-





Frequency of congenital anomalies

DZ = singletons (2-3%) MZ = risk x 3

Concordance of defects is uncommon (15% of cases)

Type of anomalies Clearly known associations

- CNS
 - Anencephaly, Holoprosencephaly
- Cardiovascular system
 - ventricular septal defect, ostium secundum type defect
- Digestive system
- tracheo-oesophageal fistula, esophageal atresia, intestinal atresia or stenosis
- Urinary system
 - Renal agenesis and dysgenesis,CKD, obstructive defects, atresia and stenosis of bladder neck and urethra
- Anomalies of abdominal wall
- Anomalies of limbs
- Anomalies of spine

Type of anomalies controversial associations

- Positional defects by intrauterine crowding
- encephalocele
- Cleft lip
- Hypospadia

Cardiac anomalies

- 3.8% prevalence in MC vs singletons
 - uncomplicated MCDA 2.26%
 - TTTS 6.90%
- The high prevalence of congenital heart disease in monochorionic diamniotic twins merits detailed fetal echocardiography

PRENATAL DIAGNOSIS Prenat Diagn 2005; 25: 403–406. Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/pd.1172

Diagnosis and outcome of congenital heart disease in fetuses from multiple pregnancies

Dario Paladini¹*, Michele Vassallo¹, Gabriella Sglavo¹, Maria Giovanna Russo² and Pasquale Martinelli¹



"We have confirmed that the diagnostic performance of fetal Echocardiography in multiple gestations is comparable with that obtained in singletons

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