



Antepartum care and prenatal diagnosis in pregnancies after IVF

Willem Verpoest
Centre for Reproductive Medicine
UZ Brussel


ESHRE Campus Lübeck 18th January 2008





Lecture overview

1. antepartum care
 1. IVF/ICSI pregnancies
 2. PGD pregnancies
2. prenatal diagnosis
 1. IVF/ICSI pregnancies
 2. PGD pregnancies



2 Verpoest UZ Brussels 18th January 2008



1. Antepartum care

IVF/ICSI pregnancies




1. antepartum care - IVF/ICSI pregnancies

increased risk of obstetric morbidity following IVF/ICSI

- miscarriage
- ectopic pregnancy
- premature delivery
- low birthweight
- infants small for gestational age
- perinatal mortality
- Instrumental delivery

Wisanto et al 1995, Aytoz et al 1998 Doyle et al 1992, Olivennes et al 1993, Buitendijk et al 2000



1. antepartum care - IVF/ICSI pregnancies

→ maternal complications controversial

- Risk increased
- Placenta praevia
 - Gestational diabetes
 - Preeclampsia

Maman 1998, Tallo, 1995

→ Risk not increased

Reubinoff 1997, Koudstaal 2000



1. antepartum care - congenital malformations

Palermo/USA	578	1.6% ¹	
Wennerholm/Sweden	1139	3.3% ²	OR 1.19 (CI 0.8-1.8) ⁶
Loft/Denmark	730	2.2% ²	
Bonduelle/Belgium	2840	3.4% ³	
Hansen/Australia	301	8.6% ⁴	RR 2.0 (CI 1.3-3.2) ⁵
Ludwig/Germany	3372	8.6% ⁵	RR 1.25 (CI 1.1-1.4) ⁶

¹ at birth major malformations

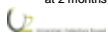
² at birth ICD 9/10

³ at birth - 2 months major malformations

⁴ at 1 year ICD 9

⁵ at 2 months EUROCAT coding system

⁶ compared to the general population



1. antepartum care - IVF/ICSI pregnancies

- obstetric morbidity following IVF/ICSI
 - Reports
 - maternal complications
 - congenital malformations
 - obstetric complications
 - preexisting disorders
 - genetic conditions
 - risk factors
 - age > 35 and delivering their first child
 - multiple pregnancy

Waterstone et al, 2001



Verpoest UZ Brussels

18th January 2008

1. antepartum care - IVF/ICSI pregnancies

- Early pregnancy
 - Follow up by fertility team up to 12/40
 - Direct referral to high risk obstetric team
- Increase awareness
- Individual risk assessment



Verpoest UZ Brussels

18th January 2008

1. Antepartum care

Preimplantation genetic diagnosis pregnancies



Centrum voor Reproductieve Geneeskunde

1. antepartum care - PGD pregnancies

● Limited data

- PGD is associated with a risk of multiple gestation, cesarean section and placenta previa
- poor statistics
→ Strom CM et al 2000.



1. antepartum care - PGD pregnancies

treatments	PGD	%	PGD-AS	%	total	%
patents	535		663		1198	
age	319		363		342	
cycles	1177	mean 22 cycles/patient	1042	mean 16 cycles/patient	2219	mean 18 cycles/patient
deliveries	205		164		369	
children	250		193		443	

PGD 1993-2004 - overall results



1. antepartum care - PGD pregnancies

treatments	PGD	PGD-AS	PGD+AS	control group	CS group	ind the group
				n=1339	n=642	
misc	23.7%	23.6%	23.7%	30.2%	31.5%	
preterm	10.75%	15.79%	13.12%	10.55%	10.08%	
placenta	15.05%	13.77%	13.69%	14.77%	13.54%	
concordance	1.43%	4.86%	3.04%	2.20%	1.92%	
TOP	0.36%	0.81%	0.57%	0.07%	0.63%	
lost to follow up					2.48%	

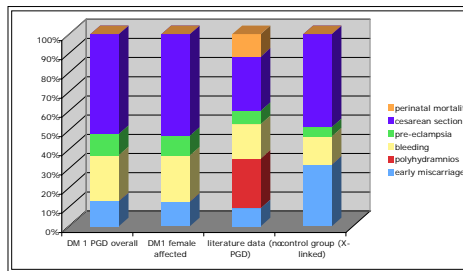


eg myotonic dystrophy



- frontal balding
- masseter, sternocleidomastoid and temporalis atrophy
- fertility issues
- obstetric risks

myotonic dystrophy complications



1. antepartum care - PGD pregnancies

- Examples
 - Osteogenesis imperfecta/achondroplasia
 - Marfan syndrome
 - Sickle cell anemia
 - Thalassemia
 - Cystic fibrosis
 - Following
 - Heart transplant
 - Renal transplant

1. antepartum care - conclusion

- preconceptional risk assessment
- preconceptional optimisation

- multidisciplinary antepartum care
 - Geneticists
 - Physicians
 - Anaesthetists
 - perinatologists



2. Prenatal diagnosis

IVF/ICSI pregnancies



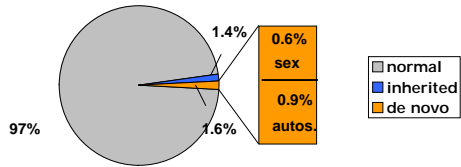
2. prenatal diagnosis - IVF/ICSI pregnancies

- the risk of finding an abnormality
 - IVF
 - ICSI
 - >36
 - >40
 - azoospermia
 - recurrent miscarriage

- the risk of miscarriage following
 - CVS
 - amniocentesis



Prenatal diagnosis in 1586 ICSI foetuses (Bonduelle 2002)



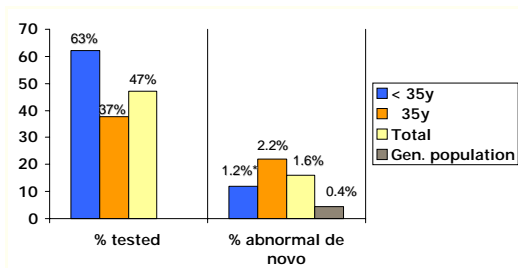
698 CVS + 892 Amniocenteses
Mean maternal age of women tested 33.5 years

Prenatal diagnosis in 1586 ICSI foetuses (Bonduelle 2002)

Abnormal results	n	%	Confidence Interval	% normal population ^{1, 2, 3}
De novo	25	1.6%*	1.02 - 2.32%	0.45 - 0.87%
Sex chrom	10	0.6%*	0.30 - 1.16%	0.19 - 0.27%
Autosomal	15	0.9%	0.53 - 1.56%	0.26 - 0.60%
Numerical	8	0.5%	0.22 - 0.99%	0.14 - 0.33%
Structural	7	0.4%	0.18 - 0.91%	0.11 - 0.22%
Inherited	22	1.4%*	0.87 - 2.09%	0.47 - 0.37%
Total	47	3.0%	2.19 - 3.92%	0.92%

¹ Jacobs et al., 1992 on 34 910 newborns
² Ferguson-Smith et al., 1984 on 52 965 prenatal samples
³ Hook et al., 1981, 1984, 1987 on prenatal samples

Prenatal diagnosis in 1586 ICSI foetuses (Bonduelle 2002)



* 1.2% CI 0.6-2.1 significantly more than in general population

Prenatal diagnosis in 1586 ICSI fetuses:
de novo anomalies, sperm parameters / origin

- Sperm count (72%)
< 20.10^6 / ml \Rightarrow 2.1 % chromosomal abnormalities (vs 0.24% > 20.10^6 /ml)
Fisher Exact 2 tailed test $p < 0.05$
- Sperm motility (83%)
< 50 % N motility \Rightarrow 1.9% chromosomal abnormalities
Fisher Exact 2 tailed test $p < 0.05$
- Sperm morphology and origin \Rightarrow no influence



Prenatal diagnosis in 1586 ICSI fetuses
(Bonduelle 2002)

Inherited abnormalities 1.4%

- Known risk related to the chromosomal anomalies in the parents (6.3%)
- 17/22 cases paternally inherited
- Preimplantation > prenatal diagnosis

\Rightarrow Informed choice of the parents
prior to the procedure



Prenatal diagnosis in 1586 ICSI fetuses
(Bonduelle 2002)

Non-inherited (*de novo*) anomalies 1.6%

- Significantly higher than general population, but absolute risk low
- Related to sperm characteristics
- Severity is variable (termination not always chosen)
 \rightarrow Sex chromosomal, structural anomalies
- Detectable from 11th week of pregnancy

\Rightarrow Informed choice of the parents
<50% agree to do a prenatal test





2. Prenatal diagnosis

PGD pregnancies



2. PGD pregnancies - prenatal diagnosis

	PGD-AS	PGD
n	272	314
Prenatal	34 (11 %)	138 (44 %)
Postnatal	56	32
Misdiagnosis	0	1(+3)



2. PGD pregnancies - prenatal diagnosis

	Indication	Pregnancy	Prenatal	Outcome
1	MD	S	affected	TOP
2	CMT1A	S	none	Born
		Tw	affected	TOP



2. PGD pregnancies - prenatal diagnosis

- Patient 1 : real misdiagnosis
- Patient 2 : erroneous linkage analysis leading to selection for affected embryos
- Misdiagnosis rate:
 - $4 / 123 = 3.2\%$ $1 / 123 = 0.8\%$
 - $4 / 249 = 1.6\%$ $1 / 249 = 0.4\%$



2. PGD pregnancies - prenatal diagnosis

	n	%
Verlinsky et al.	663	0.5
VUB	170	0.6
	314	0.3



Antepartum care and prenatal diagnosis - conclusion

- Data are inconsistent
- Overall increased risk
- Individual risk assessment
- Antepartum care: increased awareness
- Prenatal diagnosis: advice to patient and obstetrician
- PGD: multidisciplinary antepartum care

