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Graviditet och äggdonation vid TS – möjligheter och risker

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Fertility in Turner syndrome

- Spontaneous puberty 16 -30 %
- Spontaneous menarche 2-16 %
 - ad 32% among mosaics (Pasquino *et al.*, 1997)
- Spontaneous pregnancies 2-7 %
- Miscarriages ~ 30 %
- Perinatal death 7 % (Tarini *et al.*, 1998)
- Malformation rate ~ 3- 20 %

Oocyte donation (OD) - äggdonation

- First baby born in 1984
- More than 20.000 embryo transfers yearly in Europe and the United States

I Patients with ovarian failure

POF

**Ovarian dysgenesis
Surgical oophorectomy**

II Patients with functioning ovaries

Repeated IVF failures

Poor response

Endometriosis

Implantation failure

Age factor

Repeated miscarriages

Genetic disease

Oocyte donation (OD) - äggdonation

- Higher pregnancy rate per embryo transfer compared to conventional IVF (30-60%)
- Miscarriage rate similar (or slightly higher?) compared to that in standard IVF
- Higher frequency of pre-eclampsia and hypertension during pregnancy (23-38 %)
- Good perinatal outcome
- Health of the children normal (?)
- The emotional and psychosocial development of the children normal

Oocyte donation and Turner syndrome

OD results in Turner women

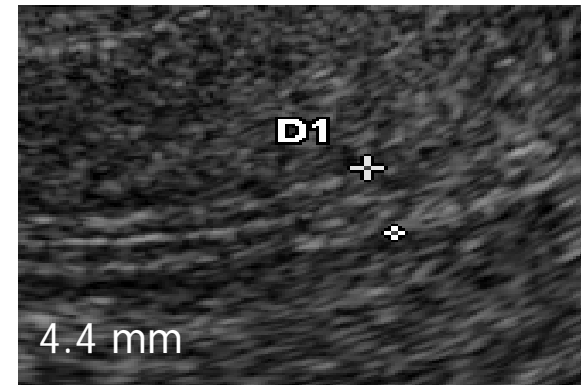
	No of subjects	No of ETs	Pregnancies Clinical PR(%)	Miscarriages (%)
Davies et al 1990	3	3	1 (33)	?
Pados et al 1992	17	43 (fresh 31)	7 (16)	0
Press et al 1995	11		6 (27)	3 (50)
Yaron et al 1996	22	58	14 (24)	4 (29)
Khastgir et al 1997	29	68 (fresh 50)	28 (41)	14 (50)
Foudila et al 1999	18	53 (fresh 28)	20 (38)	8 (40)
Delbaere and Englert 2002	9	15	5 (33)	2 (40)
Bodri et al 2006	21	30	12 (40)	3 (25)
Väestöliitto 1992-2006	28	46 (fresh)	20 (43)	7 (35)

Reason for miscarriages in TS women?

1. Chromosomal abnormalities in the fetuses
2. Diminished endometrial receptivity?
3. Inadequate endometrial preparation?
4. Uterine factors?
5. Autoimmune origin?

Turner syndrome patients lack tight junctions between uterine epithelial cells

Rogers *et al.*, Hum Reprod 1992



Oocyte donation in patients with Turner's syndrome: a successful technique but with an accompanying high risk of hypertensive disorders during pregnancy

Bodri *et al.*, Hum Reprod 2006

- 21 TS patients, mean age 33 years
- No of transferred embryos 1-4
- Clinical PR/ET 40% (12/30) + 5 biochemical pregnancies
- 10 singletons; 1 twin, 1 triplet
- Spontaneous abortion rate 25 % (n = 3)
- Premature delivery rate 50%
- IUGR 56%
- Hypertension 63 % (three cases of pre-eclampsia)
- One intrauterine death
- Mean birth weight 2789 g for singletons (1630-3790 g)
- Mean birth weight for twins 1990 ± 28 g

Oocyte donation and Turner syndrome

- risks for the mother and child?

- TS women have often cardiovascular malformations (25-50 %)
- Other health risk factors for pregnancy (hypertension, obesity)

Four deaths from aortic dissection during OD pregnancy

- Two fatal aortic dissections in pregnant TS women after oocyte donation (Nagel and Tesch 1997)
- Coarctation Aortic dissection and myocardial infarction in a pregnancy patient with TS (Garvey *et al.*, 1998)
- Coarctation of the aorta: outcome of pregnancy (Beauchesne *et al.*, 2001)
- Heart status of these four patients
 - Essential hypertension and a mildly dilated aortic root
 - Essential hypertension
 - Surgical repair of aortic coarctation
 - No prenatal risk factors identified

Risk of death in pregnancy achieved through oocyte donation in patients with Turner syndrome: a national survey

Karnis MF *et al.*, Fertil Steril 2003

- Contact to all 258 donor-egg programs in the USA
- 144 (52%) programs reported 146 patients treated, resulting in 101 pregnancies
- One patient died from aortic rupture while awaiting treatment
- 72 (49%) patients were pre-screened with echocardiography
- A literature review identified four case reports of TS who died during the same time period

- **CONCLUSION:** The maternal risk of death from rupture or dissection of the aorta in pregnancy may be 2% or higher.

Increased maternal cardiovascular mortality associated with pregnancy in women with TS

The Practice Committee of ASRM; Fertil Steril 2006

- The risk of death during pregnancy may be increased as much as 100-fold for women with TS
- Cardiology consultation and careful screening is a prerequisite for any planned attempt at pregnancy via OD
- A echocardiogram revealing any significant abnormality represents an absolute contraindication to attempting pregnancy
- Women with TS having a normal echocardiogram who intend to attempt pregnancy require careful observation and frequent formal reevaluation throughout gestation.

Care of girls and women with Turner syndrome: A guideline of the Turner Syndrome study group JCEM 2007

- "A history of surgically repaired cardiovascular defect, the presence of BAV, or current evidence of aortic dilatation or systemic hypertension should probably be viewed as relative contraindications to pregnancy"
- "Women with cardiovascular issues (BAV, dilated aorta, or history of coarctation) are best counseled against attempted pregnancy."

Oocyte donation in Väestöliitto Fertility Clinic

- Both known and anonymous donors
- Waiting time 1.5-2 years for anonymously donated oocytes
- One anonymous donor – two recipients
 - if 10 or more eggs are collected
- ART law in Finland 1.9.2007
 - Registration of identifying information of all donors

OD programme in Väestöliitto Turner patients

- Exclusion of medical contraindications for pregnancy
- Prepregnancy evaluation by a cardiologist, echocardiography
- During waiting time careful blood pressure follow-up
- Yearly lab: hemoglobin, blood glucose, thyroidea and liver function
- “Test HRT cycle” – adequate hormonal RT 4-6 months before the planned ET
- Hysterosonography/hysteroscopy to exclude uterine anomalies

Hormone replacement therapy in OD patients

- Estradiol valerate 4-6 mg/day for 12-16 days
- Vaginally micronized progesterone (Lugestron) 600 mg/day started on the day of the donor's oocyte collection

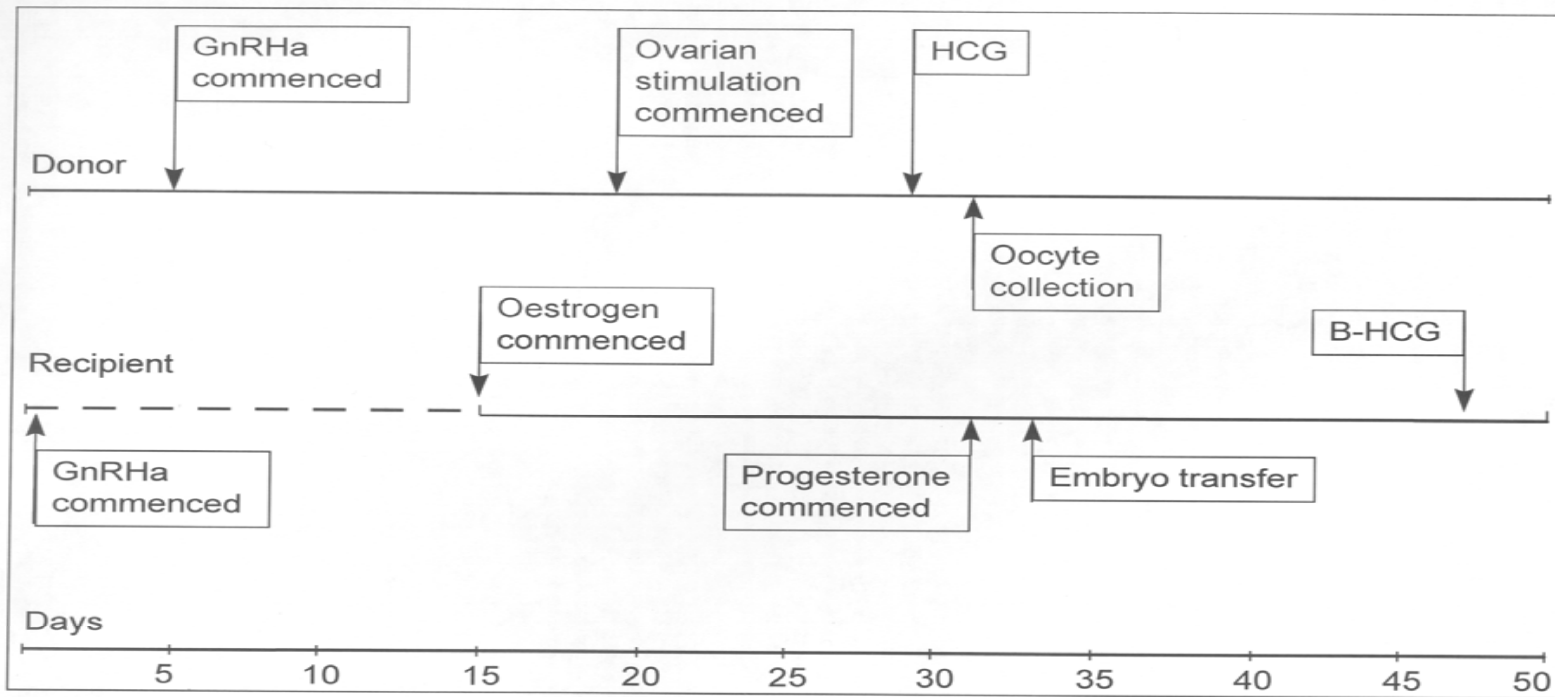


Figure 1. Synchronization of donor and cycling recipient using GnRH agonist

(According to Davies, 1992)

OD treatment of Turner women in Väestöliitto

Turner's syndrome and pregnancies after oocyte donation

Foudila *et al.*, Hum Reprod 1999

OD-results 1992-1998

OD-data **after SET** in Turner patients 1999-6/2008

Obstetric and perinatal outcome in Turner patients

Helsinki, Turku, Oulu

1992-2006

Turner syndrome and OD outcome

	1991-1998 ¹
TS patients with fresh ET	17
Mean age of patients (yrs)	29 (21-38)
No of oocytes received/patient	12.3
No of fertilized oocytes per recipient	6.9
Mean number of transferred embryos	1.8
Clinical PR/ET (%)	46.4 (13/28)
No of miscarriages	7 (54%) ²
Delivery rate /ET	21.4 %

¹ Foudila *et al.*, Hum Reprod 1999

² Termination of a vanishing twin pregnancy because of encephalocele

SET in oocyte donation (fresh transfer)

	All oocyte recipients 2000-2004*	Turner patients 1999-6/2008
No of fresh embryo transfers	102	24
No of transferred embryos	1.0	1.0
Clinical PR/ET	41.2 %	37.5 %
Delivery/ ET	30.4 %	33.3 %

*Söderström-Anttila *et al.*, RBMOnline 2007

Outcome after OD in Turner syndrome 1992-2007

Väestöliitto Helsinki, Turku, Oulu

- **Live birth/fresh ET 32.8 %**
- **Live birth/frozen ET 15.3%**
- **Live birth/treated patient 76.3%**

Obstetric complications after OD in TS

Väestöliitto, Helsinki, Turku, Oulu (n = 31)

- Pregnancy induced hypertension 25.8 % (8/31)
(mild PE 3, severe PE 4, essential hypertension 1)
- Gestational diabetes 9.7 %
- Hepatogestosis 9.7 %
- Cesarean sectio 87%
- Duration of pregnancy 31+5 - 42+0 weeks
- Preterm delivery 13 % (31+5; 34; 36+0; 36+1)
- Placenta accreta in the twin pregnancy

Pregnancy outcome after OD in Turner patients

Väestöliitto 1992-2007

- 34 infants born
- Mean birth weight singletons 3044 g (range 1020g-4200g)
- Birth weight twins
 - 2130g/2810g
 - 2470/2280g
- SGA babies 12 % (4/34)
 - Singletons 7 % (2/30)

Graviditet och äggdonation vid TS – möjligheter och risker?

- Möjligheterna mycket goda för graviditet med äggdonation
- Riskgraviditet både för mamman och barnet

Graviditet och äggdonation vid TS – riskminimering

- Noggrann kardiologisk utredning och uppföljning under graviditeten
- Avrådande av behandling ifall av hjärtabnormalitet (“A history of surgically repaired cardiovascular defect, the presence of BAV, or current evidence of aortic dilatation or systemic hypertension **should probably be viewed as relative contraindications** to pregnancy”).
- ”Prepregnancy” omhändertagande: RR-uppföljning, viktreducering, thyreoideastatus
- Flerbördsgraviditet kontraindikation
- Noggrann obstetrisk uppföljning