



Fertility issues and pregnancy outcomes in Turner syndrome

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Turner syndrome

- **1:1,700** newborn females babies
 - The most common sex chromosomal disorder in female
 - Primary ovarian failure
 - short stature
 - complex cardiovascular phenotype
 - Metabolic and autoimmune abnormalities
 - Infertility
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Fertility

- Spontaneous pregnancy
 - Fertility preservation
 - Oocyte donation In vitro fertilization (OD - IVF)
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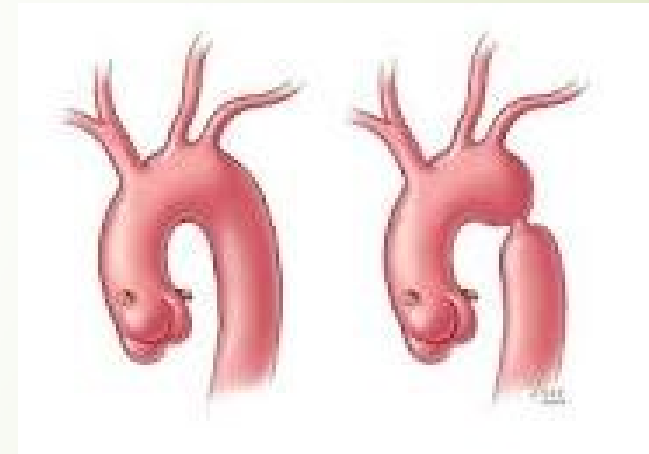


Increased risk of complications in pregnancy

- ▶ early pregnancy loss
 - ▶ pregnancy induced hypertensive disorders
 - ▶ preterm delivery
 - ▶ Fetal congenital abnormalities
 - ▶ abnormal karyotype in TS with spontaneous pregnancy
 - ▶ risk of maternal death 2% due to aortic dissection
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Conditions associated with aortic dissection

- bicuspid aortic valve
- aortic coarctation
- aortic dilatation
- hypertension





M & m

- Retrospective study in 156 women with TS

- Outcome measurements:

Parenting choices: Spontaneous / assisted pregnancies

Maternal pregnancy complications: Miscarriage, PIH, GDM

Aortic dimension changes related to pregnancy

Mode of delivery

Neonatal data: Gestational age at delivery, birth weight, Apgar scores, diagnosis of TS in female offspring



Aortic dimension changes



Ascending aortic size index

$\geq 20 \text{ mm/m}^2$: moderately dilated aorta

$\geq 25 \text{ mm/m}^2$: severe dilatation



Conditions associated with poor pregnancy outcomes

age >35 years

BMI >35 kg/m²


abnormal thyroid function

hypertension

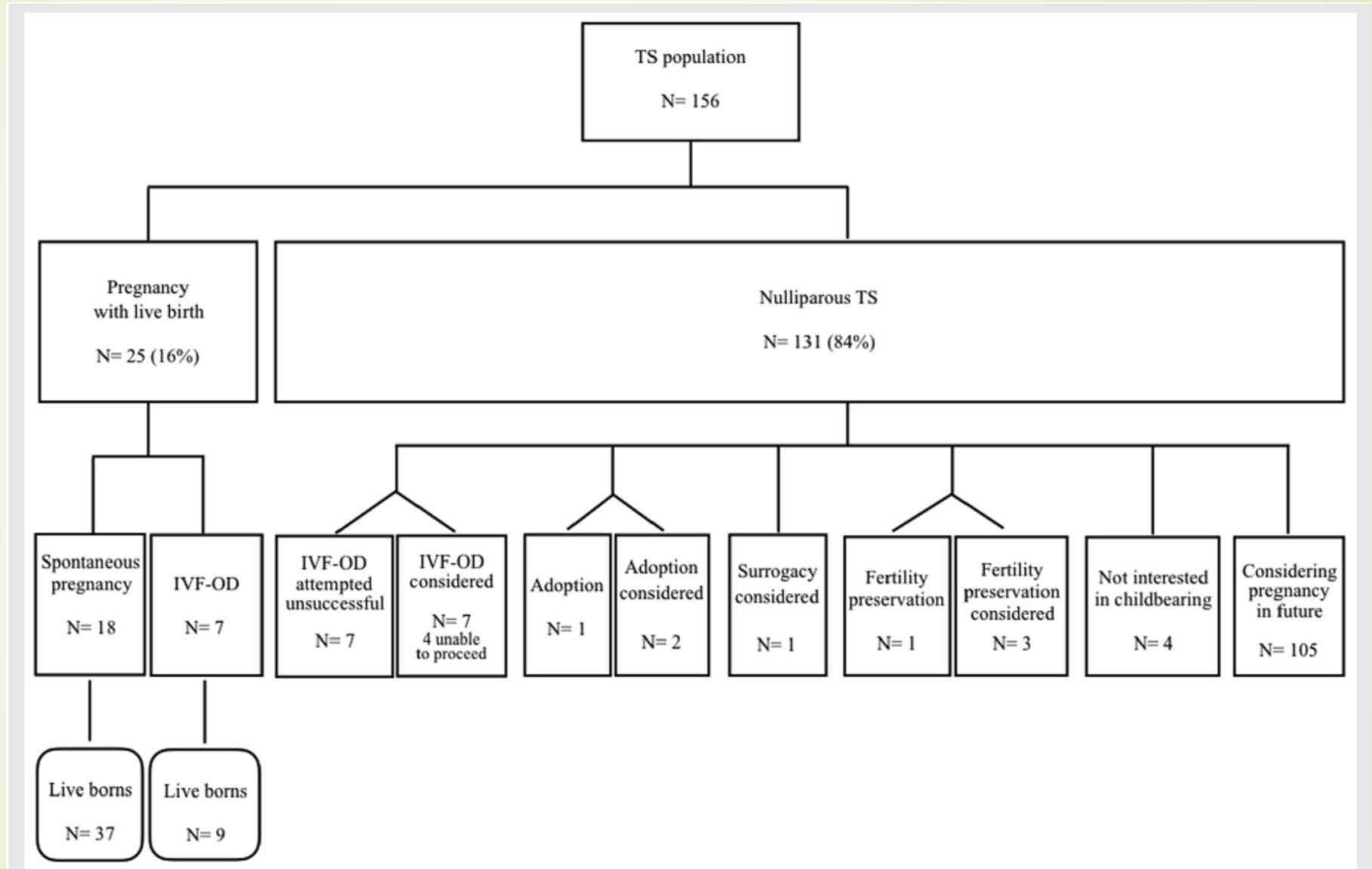
cardiovascular conditions: bicuspid aortic valve, aortic dilatation,
aortic coarctation, aortic surgery



Pregnancy should be avoided in

- **Ascending ASI >25 mm/m²**
 - **ASI >20 mm/m² with associated risk factors for aortic dissection**
 - **history of aortic dissection**
 - **long-term impact of pregnancy on TS-related comorbidities**
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RESULTS



Parenting choices and fertility outcomes in Turner syndrome. IVF-OD = in vitro fertilization oocyte donation.

Calanchini. *Fertility in Turner syndrome. Fertil Steril* 2020.





Spontaneous Pregnancy

- ▶ 18 women / 66.7% had more than one pregnancy / a total of 37 newborns
- ▶ mean age at first SP was 23.5 years (15–31 years)
- ▶ patients were diagnosed with TS after
 - The first pregnancy (n= 4)
 - Miscarriages (n= 2)
 - Secondary amenorrhea (n= 1)
 - Diagnosis of TS in her daughter who experienced miscarriages (n= 1)

Women with SP

- ▶ 61.1% had a karyotype with **more than one X** / 3.2% (2/62) with **45,X**
47.8% (11/23) with **45,X/46,XX**
- ▶ All women with SPs had spontaneous menarche and regular menstrual
spontaneous menarche was a predictive factor of spontaneous conception ($P < .001$)
- ▶ 47.6% first trimester miscarriages
- ▶ Associated: gestational diabetes, preeclampsia
- ▶ Not associated: liver and thyroid function test abnormalities

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- ▶ The indication for elective cesarean delivery was mainly for increased maternal risk of aortic dissection
 - ▶ Of livebirths, 72% were female
 - ▶ Karyotype was checked in 4 cases : all normal karyotype
amniocentesis (n= 2) , test at birth (n= 2)
 - ▶ One daughter with TS was detected in adulthood after experiencing miscarriages; the karyotype of her and her mother was 45,X/46,X ring.



Assisted Pregnancy

- IVF-OD: 14 pts/ 39 cycles
- pregnancy with in half of them
- success rate per cycle of 17.9%
- 30.8% were 45,X and
- 38.5% had a karyotype with Y-chromosome material
- All 11 women with Y-chromosome material underwent bilateral gonadectomy



DISCUSSION

- Prevalence of SP: 14%
- live birth: 12% for SP (in previous studies the prevalence ranging from 2% to 8%)
- main predictive factors for SP:
 - Spontaneous menarche
 - 45,X/ 46,XX karyotype
- Suggestion: presence of a 47,XXX cell line confers a higher chance of conceiving
- two women with monosomy X having SP with live birth
 - considering that a 45,X karyotype in peripheral blood leukocytes does not preclude the coexistence of 45,X/46,XX mosaicism in the ovary

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- ▶ unplanned pregnancy in previously diagnosed women with TS

Emphasize the importance counseling for all women with TS about the use of contraceptive methods






Counseling



- ▶ **cryopreservation of mature oocytes** is promising option in young TS girl presenting with spontaneous menarche, regular menstrual cycles and normal antimullerian hormone levels
- ▶ paucity of data in TS on reliable markers of follicular ovarian status
- ▶ **it is recommended to avoid oocyte retrieval before the age of 12 years**
- ▶ **Ovarian tissue cryopreservation** is feasible at younger ages but it requires an operation and anesthesia
- ▶ **Adoption** as an option for parenting in few women
- ▶ Importance of early counseling regarding the possibility of fertility parenting alternative options




Maternal and Fetal Outcomes

- Higher rate of miscarriage in TS (48% of spontaneous conception)
 - High rate of pregnancy loss in TS with IVF-OD
 - compromised endometrial receptivity due to hypoestrogenism
 - higher prevalence of thyroid autoimmunity disease
 - IVFOD with double embryo transfer is associated with miscarriages and poor maternal and fetal outcomes.
 - Fetal chromosomal abnormalities
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- ▶ Young women with TS are susceptible to
 - Increased BMI
 - metabolic disorders
 - liver biochemical abnormalities
 - PIH
 - ▶ prevalence of preeclampsia was 11% in SPs, while no patients who had OD experienced preeclampsia, despite the fact that these women were older and had more cardiovascular risk factors

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- Higher prevalence of female offspring after SP
 - pregnancy in TS is the increased prevalence of cardiovascular complications
 - In TS, aortic dissection occurs at a younger age
 - It is mandatory to extensively evaluate the risk for aortic dissection at preconception and to transfer a single embryo after IVF to minimize complications

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- There is a debate regarding the aortic root diameter above which pregnancy should be discouraged in TS
 - Aortic diameters measured at SoV and ascending aorta increased during pregnancy and postpartum
 - The aortic growth rate related to pregnancy was higher compared with that in nulliparous TS
 - Ascending ASI >20 mm/m₂ as a cutoff for considering TS patients at higher risk of aortic dissection in pregnancy, especially in the presence of other risk factors for aortic dissection.
 - Studies report no excess mortality and TS-related comorbidities in the years postpartum




study limitation

- ➔ it is a retrospective study

Conclusion

- Higher rate of SP pregnancy than previously reported
- Predictors of SP: Spontaneous menarche, 2nd or 3rd cell line with more than one X
- Counseling for women with TS regarding fertility options
 - Fertility preservation
 - Alternative parenting options
 - Prenatal genetic testing
- The potential for SP needs to be clearly explained, and therefore the possible requirement for contraception
- Full discussion of the maternal and fetal risks related to pregnancy
- At preconception, an extensive assessment of the risk factors for aortic dissection and poor maternal and fetal outcomes



This study highlights the importance of a TS-dedicated **multidisciplinary management** of pregnancy, before and during pregnancy and in the postpartum

