سلام گرم منو پذیرا باشید🌸
روزتون پراز نشاط💗

Screening & diagnosis of chromosomal defects in multiple pregnancy

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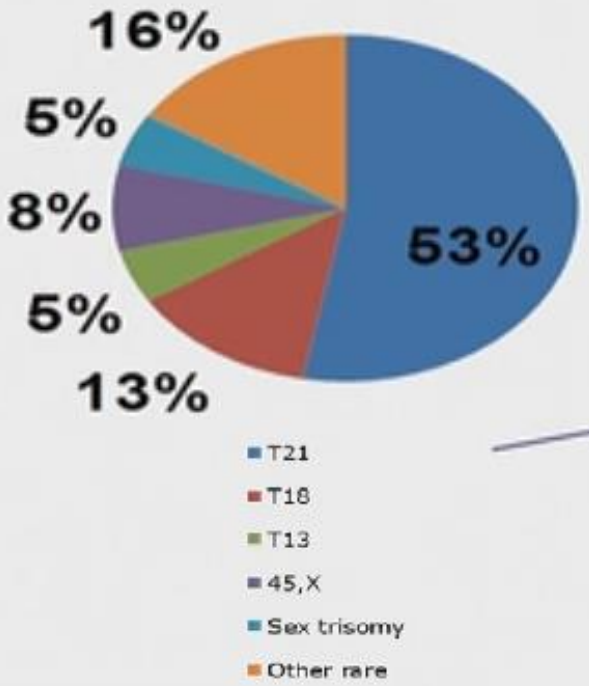
Grades of recommendations

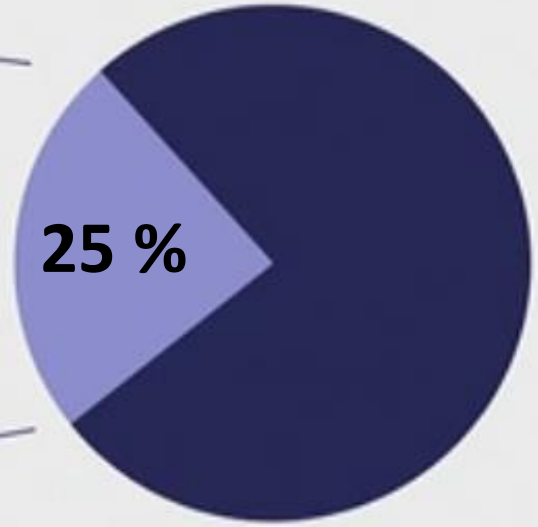
A	At least one meta-analysis, systematic review or randomized controlled trial rated as 1++and applicable directly to the target population; or systematic review of randomized controlled trials or a body of evidence consisting principally of studies rated as 1+applicable directly to the target population and demonstrating overall consistency of results
B	Body of evidence including studies rated as 2++applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++or 1+
C	Body of evidence including studies rated as 2+applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence of level 3 or 4; or evidence extrapolated from studies rated as 2+
Good practice point	Recommended best practice based on the clinical experience of the guideline development group

Prenatal prevalence of genetic abnormalities

Chromosomal



Sub-chromosomal



Microdeletions
Copy-number variants
(CNV)

Screening for chromosomal abnormalities in twin pregnancy

• Screening for trisomy 21 can be performed in the first trimester using the combined test (NT, free β-hCG & PAPP-A level). • An alternative is combination of maternal age and NT only	B
• In case of a vanished twin, if there is still a measurable fetal pole, NT alone, in combination with maternal age, should be used for risk estimation 21	B
• The detection rate (DR) of non-invasive prenatal testing for trisomy 21 may be lower in twins than in singletons, but data are still limited	B

The problem of the vanishing twin

Rate of vanishing twin from 7 weeks: 15%

Placenta of vanished twin continues to shed cfDNA

Vanished twin more likely to have abnormal karyotype

Most companies / hospitals do not accept cfDNA samples in pregnancies with a vanished twin

Invasive testing in chromosomal abnormalities in twin pregnancy

• The likelihood of being offered invasive testing on the basis of a combined screening result is greater in twin compared with singleton pregnancy	2++
• Invasive testing carries greater risks in twin: - 2% following CVS - 1.5–2% following amniocentesis	2++

Twin Pregnancy: aneuploidy

Complexity of Screening & and diagnostic testing for trisomy in twins

• Screening and diagnostic testing for trisomy is **more complex** in twin compared with singleton pregnancy. • It is important, therefore, that counseling prior to testing is provided by healthcare professionals with expertise.	2+
• It is important to **inform women and their partners** in advance of the potentially complex decisions on the basis of the results of combined screening: - The increased risk of invasive testing in twins - The possible discordance between dichorionic twins for fetal aneuploidy - The risks of selective fetal reduction	2+

Screening for chromosomal abnormalities in twin pregnancy

Cell-free DNA (cfDNA)

• Analysis of maternal blood for risk assessment for fetal trisomy 21 is used increasingly in clinical practice. • It has a much higher DR and lower FPR than does the combined test • In a recent meta-analysis, the weighted pooled DR for trisomy 21 in singleton pregnancy was 99% for a FPR of 0.1%28. The corresponding values in twin pregnancy were 94.4% and 0%.	2++
• However, so far, the reported number of trisomy-21 cases in twin pregnancy diagnosed using cfDNA testing is far smaller than that in singleton pregnancy	2++

Invasive prenatal diagnosis in twin pregnancy

• CVS is preferred in dichorionic twin pregnancy because it can be performed earlier than can amniocentesis	D
• Earlier diagnosis of any aneuploidy is particularly important in twin pregnancy, given the lower risk of selective termination in the first compared with the second trimester	2++
• Invasive testing for chromosomal or genetic analysis of twins should be carried out by a fetal medicine expert.	
• It is important to map carefully the position of the twin in the uterus	

Invasive prenatal diagnosis in twin pregnancy

• If chorionicity has been confirmed before 14 weeks' gestation and the fetuses appear concordant for growth and anatomy, it is acceptable to sample only one amniotic sac. • Otherwise, both amniotic sacs should be sampled	3
• CVS in monochorionic pregnancy will sample only the single placenta so will miss these rare discordant chromosomal anomalies.	
• When monochorionic twins are discordant for an abnormality, prior to invasive testing a discussion should take place regarding the complexity of selective termination, should it become necessary	

Screening for structural anomalies in twin pregnancy

• In around 1 in 25 dichorionic, 1 in 15 MCDA and 1 in 6 monoamniotic twin pregnancies, there is a major congenital anomaly that typically affects only one twin.	3
• At the first-trimester scan (between 11+0 and13 +6 weeks' gestation) the fetuses should be assessed for the presence of any major anomalies	
• Routine second-trimester ultrasound screening for anomalies in twins should be performed by an experienced operator at around 20 (18–22) weeks' gestation. (takes time about 45')	

Screening for structural anomalies in twin pregnancy

• Cardiac screening assessment (echocardiography) should be performed in monochorionic twins	3
• Abnormalities associated with twins include - neural tube defects - anterior abdominal wall defects - Facial clefts - Brain abnormalities - Cardiac defects - Gastrointestinal anomalies	

Managing twin pregnancy discordant for fetal anomaly

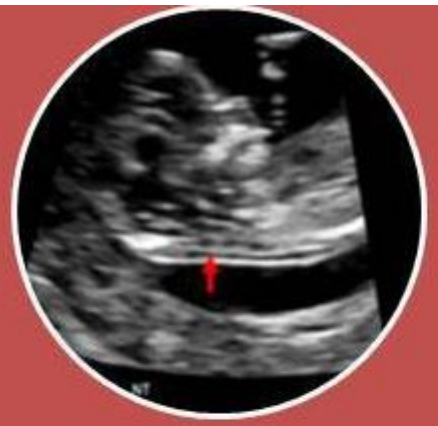
• Twin pregnancies discordant for fetal anomaly should be referred to a regional fetal medicine center.	✓ .
• The management is different according to chorionicity	

In twin pregnancy there is always a foot print of chorionicity

Complication	DC	MC
Miscarriage at 11-13 w	2%	10%
Perinatal death at ≥ 24 w	2%	4%
Growth restriction of ≥ 1 fetus	20%	30%
Preterm delivery < 32 w	5%	10%
Major defect	1%	4%

In twin pregnancy there is always a foot print of chorionicity

Current screening methods for Down syndrome



11-13 wks
NT
NT-Combined
1T UT

15-19 wks
Quad
Contingent/Integrated
2T UT

3T

	DR	FPR
DC	About 90%	3% /f 6%/p
MC	87.4	8 %

	DR	FPR
Singleton	99%	1%
Twins	94.4	0%

NIPS (after 9 wks)

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Take home massage

- **Determination of chorionicity** has the major role in management of twin pregnancy: (**please note to clear documentation & save it**)'
- Clear mapping of twins is an essential item especial for later intervention. (**please note to clear documentation & save it**)
- According to our national guideline : consider **the 1th trimester combined screening test as screening test for chromosomal abnormality in twin pregnancies** (exception: vanished twin)
- Cell free DNA is the most predictive screening test for down syndrome screening. But the data are limited yet.
- Consider fetal echocardiography in the management of MC twins pregnancy at about 18-20 wk.
- Discordance chromosomal or congenital abnormalities is a challenging subject : please consider a clear and precise counselling with parents.