Obstetrics & Gynecology
TEAM

Prenatal Testing

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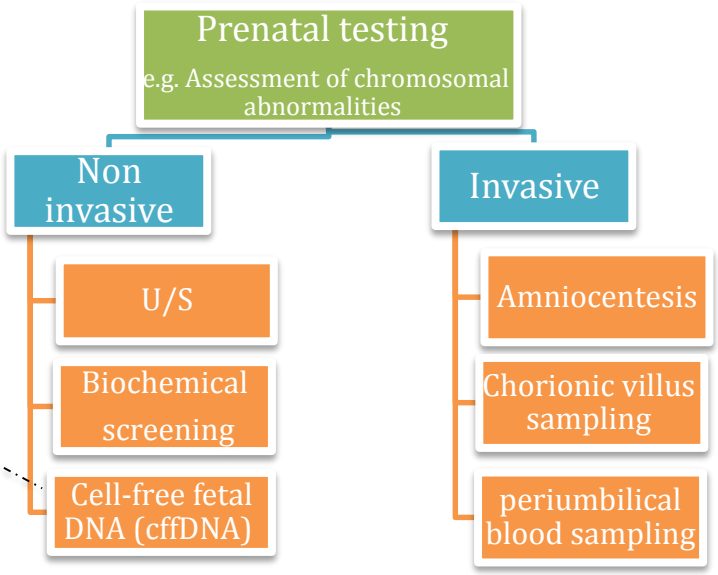
Everything written below was mentioned by the doctor (Slides are not available for this lecture)

Prenatal Testing

Testing for fetal wellbeing during pregnancy.

E.g. chromosomal abnormalities, structure of the baby.

Cell-free fetal DNA is considered noninvasive although it's drawn from the mothers' blood. In this case when we say noninvasive we're referring to whether it's invasive to the pregnancy itself or not



Methods available for screening for chromosomal abnormality

1- **Age of the mother :**

An old method in which screening was by the age of the mother only for e.g. if the mother is 35 she would be told that te incidence is high (This method is highly nonspecific and the false positive rate was very high

2- **Biochemical markers** : PAPPA&β HCG biochemical markers (Explained below)

Biochemical markers were developed in order to be more specific than the first method. However, they were not very specific

3- **U/S :**

Ultra sound measurement Nuchal translucency (N.T) + others (Explained below)

4- **Fetal DNA:** Free fetal DNA in maternal blood (Explained below)

The ideal screening is to do both U/S Nuchal translucency with PAPPA&β HCG biochemical markers to lower the false positive rate. (The doctor mentioned that biochemical markers are not done at KKUH)

General Facts: (The doctor said the facts are important and usually they get it in MCQs)

- The general incidence of Down is 1:1000
- The risk by maternal age:
  - at the age of 35 ----------1:365
  - at the age of 40----------1:109
  - at the age of 45----------1:32
- Risk of recurrence is 1% (0.75% higher than maternal age related risk
- In case of parental aneuploidy : 30% risk of Trisomy in offspring. (e.g. When the mother or the father is a carrier of an abnormal chromosome)

1- Ultrasound screening for chromosomal abnormality

Nuchal translucency (N.T): (The most important way in screening and the most commonly used, it's also the easiest)

Skin fold thickness behind the fetal cervical spine.

- Timing: **11-13** $^{+6days}$ weeks of pregnancy. (timing is very imp because if you miss the time it might return to normal at later weeks)
- 75-80% of trisomy 21
- 5-10% normal karyotype (but could be associated with cardiac defects, diaphragmatic hernia, Exomphalos)

Which means it might be seen although the fetus has no chromosomal abnormalities. That's why when it is seen we move to the next step to confirm with amniocentesis or cffDNA

Markers other than N.T :

- Nasal bone: If you can see the nasal bone it means the fetus is okay if there is a short nasal bone the risk of chromosomal abnormalities is very high.
- Frontomaxillary angle : the same idea as nasal bone (usually people with Down syndrome or other chromosomal abnormalities have flat face)
- Blood flow in ductus venosus (If you are an expert you can measure) → If abnormal there is high risk of chromosomal abnormality.

If the doctor would like to screen using one of the three points mentioned. The screening should be at the same gestational age for N.T screening (11-13 weeks)

2- Biochemical Screening

So if you find low PAPPA and normal nuchal translucency you still label the patient as high risk because she can develop IUGR ..etc

1st trimester At week 10 of pregnancy	
PAPPA: Low level is associated with chromosomally abnormal fetus. Low levels are also associated with IUGR , preeclampsia and abortion	From the mother blood
β HCG: If you find it too high for the gestational age , the risk is very high to develop chromosomally abnormal baby	

2nd trimester
Triple & quadruple Test

3- Amniocentesis

Obtaining a sample of amniotic fluid surrounding the fetus during pregnancy

Indications	
Diagnostic (at 11- 20 weeks) usually its done at 16weeks , the earlier it's done the more complications it causes)	**Therapeutic** (At anytime)
1. Chromosomal analysis (Down syndrome) 2. Spina bifida (Alpha fetoprotein) 3. Inherited diseases (muscular dystrophy) 4. Bilirubin level in isoimmunization 5. Feta l lung maturation (L/S ratio)	1. Reduce maternal stress in polyhydramnios 2. Mainly in twin-twin transfusion or if abnormality associated

Complications

1- Abdominal cramps
2- Leak or rupture membrane
3- Risk of abortion 1: 200
4- Bleeding
5- Infection e.g. chorioamniotis .
6- Injury by the needle.
7- If done therapeutically, the amount of fluid will be reduced and the fetus will be at risk of developing Club foot.

If you suspect the mother is having an infection for e.g. toxoplasma and you want to know if the fetus is infected or not you can do amniosentesis (if she's in first trimester so pregnancy can be terminated).

4- Chorionic Villus Sampling (CVS)

Sampling is done to the cyto-trophoblasts (**not syncitiotrophoblast**)

Indications for CVS	
Fetal karyotyping	**Genetic testing**
1. Advanced maternal age 2. Abnormal first trimester biochemical screen 3. Ultrasound findings 4. Personal and family history of trisomy 5. Abnormal parental karyotype	1. Family history of single gene disorder 2. Cystic fibrosis 3. Duchenne muscular dystrophy 4. Osteogenesis imperfecta

- Done between 10-14 weeks of pregnancy
- Risk of abortion : 1:100 (higher than amniosentesis)
- If the mother is Rh – if willing to do any procedure should be given anti D
- False rate : 1 % (because of the mixture in the placenta between maternal and fetal blood, so it can be the mothers' blood)

5- **periumbilical blood sampling**

Obtaining blood from umbilical cord during pregnancy.

It is done at the insertion of the umbilical cord into placenta to prevent bleeding .

Indications	Complications
1- Genetic testing. 2- If the patient needed screening but presented too late for nuchal translucency or amniocentesis or the patient is oligohydromnious and can't do amniocentesis . 3- If you're suspecting that the fetus is infected, it can be performed to confirm the infection 4- Low fetal hg or blood level (fetal anemia). So blood transfusion can be done through umbilical cord .	1-Fetal bradycardia. 2-Intrauterine death 3-Umbilical artery spasm **Due to its complications:** 1- It is performed in the delivery room 2- Dexamethasone is given for maturation of lung of the fetus. 3- Neonatal intensive care is prepared to take the baby in case of delivary 4- OR is prepaired for C-section

Noninvasive prenatal testing:

6- Cell-free fetal DNA

Free fetal DNA in maternal blood

- A sample of maternal blood ,where DNA of the fetus is separated from
- Allows to know the age of the fetus , blood group, any type of abnormal genes and sex.
- Can be done as early as 10 weeks .

Indications	
Detect chromosomal Abnormalities	Know the sex of the fetus
Know fetus blood group	Myotonic dystrophy
Beta thalassemia	Autosomal recessive disorders
Autosomal dominant disorders	Huntington disease
Cystic fibrosis	

In addition to the DNA of the current fetus you can also find DNA of previous fetuses and tell how many times the woman got pregnant and know more information about each fetus

Results should be available in two weeks

It's very expensive

An Alternative for all previous testing mentioned above!

Preimplantation genetic diagnosis:

Diagnosis of an embryo by IVF to know whether it's a carrier or have any abnormal gene or chromosome before implanting it in the mother.