Course Name :An Overview on Maternal Health Antenatal, Intranatal and Postnatal Care

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Invasive and non-invasive Prenatal Diagnostic test (contd.)

Hello students. I welcome you all to yet another session for the NPTEL online certified course on the topic and overview on maternal health, the antenatal, intranatal and postnatal care. I am Dr. Barnali Ghosh, an obstetrician and gynecologist working as assistant professor at B.C.Roy Medical College and Medical Research Center, IIT, Kharagpur. So today we will be continuing our discussion regarding the prenatal diagnostic tests right.

So we have discussed the invasive tests or the different invasive methods that is the cordocentesis, the sorry first coming from the beginning the chorionic villus sampling, the amniocentesis and the chordal synthesis. These are all the diagnostic tests which confirm that yes the baby is anomalous and then you need to counsel the parents regarding whether to continue the pregnancy or to go for termination. Now coming to a very important new concept coming into the picture now in today's scenario which is a non-invasive method right. This non-invasive method is actually using the cell free fetal DNA, cell free fetal DNA in the mother's plasma.

So from the name itself you can deduce that know from the mother's plasma or serum that is in the mother's blood circulation. Thus fetal DNA, the fetus, the fetal cells and the fetal DNA they know they are coming to the amniotic fluid, they are desquamated in the amniotic fluid and from the amniotic fluid it can pass on to the maternal circulation. And just by taking the maternal blood we can know segregate the fetal DNA and from these fetal DNA we can assess the genetic structure of the fetus and whether there is any anomaly, whether there is any change in the chromosome number as in aneuploidies, whether there is any mutation point mutation or single gene deletion right leading to certain genetic disorders as in cystic fibrosis, Tay Sach's disease, BRCA mutation right these all can be assessed right and also the RH status of the baby very very important RH whether the baby is RH positive or RH negative and this is particularly important to know if the mother has a RH negative blood group right. So, coming to the non-invasive NIPT what is shown in this picture you can see yes the fetus, the fetal cells know they get desquamated inside the amniotic cavity. These are the fibroblastic cells there may be certain fetal DNA fragments inside the amniotic cavity, the amniotic fluid and from this

amniotic fluid it will pass on through the placental circulation into the maternal blood stream.

So, these red color these are the fetal DNA and the blue the blue are the maternal DNA sorry. So, these blue are the maternal DNA right. So, how to differentiate actually maternal DNA are longer they are longer right whereas, fetal DNA, fetal DNA these are shorter. So, from that we detect the fetal DNA in the maternal circulation and very important question whether it is a screening test or a diagnostic test yes it is a screening test, but this screening test has a very high specificity and sensitivity it has high as high as 99 percent specific. So, that means, if the test comes as negative.

So, you can jolly well say that yes the fetus is a normal fetus as the specificity is 99 and some books even say 99.5 percent approximately it is approaching towards 100 percent. So, view it is a very good test in our hands without going for the invasive procedures without going into the complications of the invasive procedures we can you know detect fetal anomaly from this test. Next is the timing when to go for the NIPT it can be done anytime from 10 weeks onwards right up till term and what is the origin I have already told the fetal fibroblast right fetal fibroblast, fetal lymphoblast or lymphocytes granulocytes, fetal red blood cells all these come into maternal circulation right. So, these are the origin of the cell free fetal DNA and sometimes you know fetal DNA loose fetal DNA will be circulating in the maternal circulation loose fetal DNA right.

So, this are the origin of the test NIPT. Now percentage what is the percentage of fetal DNA that is in present in the maternal circulation it is approximately 3 percent. So, here is the most important point that fetal DNA is only 3 percent you know in the first trimester in the early weeks in the first trimester around 10 weeks. So, it is only 3 percent. So, out of the all the maternal circulation you have to check for the fetal DNA and it increases to 6 percent at term right.

So, actually it is 3 percent of fetal DNA versus 97 percent of maternal DNA. So, it is a laborious task, it is a labor some process which will take time, it will take patience and it will you know need the it needs the examiner to patiently look into the slide and search for the fetal DNA then only the test will have that accuracy right. So, even for blood cells fetal blood cells if you say the fetal whole blood cells, the whole fibroblast or whole lymphocyte or whole red blood cell of fetal origin coming into the maternal circulation it is ratio is 1 is to 1 to 10 million. So, in 1 in 10 million cells of mother, in 10 million maternal cells only one fetal cell is present right. So, only one fetal cell.

So, you need to be very patiently looking into the slide and detect the fetal cell and from that fetal cell you will extract the DNA and go for the genetic test. So, what are the indications? The where we go for NIPT? Number 1 with the patients with intermediate risk. So, you know fetal and maternal foundation, the fetal maternal medicine fetal medicine foundation right those

people have segregated into low risk, intermediate risk and high risk. High risk definitely will directly go into the invasive test, but the intermediate risk that is coming in between 1 is to 100 to 1 is to 1000. So, this intermediate risk when the risk ratio of the first trimester screening test is between 1 is to 100 to 1 is to 1000 they are the intermediate risk and they need to go for NIPT.

Number 2 if there is a high risk patient and she does not want high risk mother right with screen positive result of the first trimester and she does not want to go for invasive test. Because of the risk of complication and fetal loss then also you can advice her NIPT. Since she finds any anomaly right there is history of previous trisomy 21 in previous pregnancy. Parents are having balanced translocation and I have already told RH negative pregnancy. So, in all these cases we can go for NIPT.

Why? Because this will for the screen right RH negative pregnancy meaning that only 50 percent we need to first assess the father. Yes, the father is RH positive so that means, the fetus there is a risk for the fetus for being RH positive, but that does not mean that 100 percent of the fetuses will be RH positive. So, if we go for NIPT and if we take the fetal cells right in the maternal blood and we check for the RH status of that fetus right. So, if the fetus is RH negative then no need to bother right no need to go for anti-dimino globulin because that will also risk these injections given to the mother empirically or prophylactically will risk and will have the risk of prions disease. So, if from this test we can assess the fetal blood group and if it is RH negative no need to go for these further injections.

If it is RH positive then yes definitely you need to you know further you know go for evaluation the markers right the different markers which are present in RH negative pregnancy you need to evaluate and also evaluate the baby. So, this way it makes our work easier and this is a very important test which can be done in the maternal plasma, but to keep in mind that it is very very costly right it is very costly you know around 30 to 50,000 cost will come and so you need to segregate and you know ask for NIPT only for those high risk cases who need NIPT right not done routinely. And what is the detection rate is I have told that it is 99 percent sense specific. So, that means, that the negative predictive value is very high, high negative predictive value. In high risk group in high risk group the positive predictive value is approximately 83 percent.

In low risk group low risk group negative predictive value is again 99 percent and positive predictive value is 33 percent. So, from this you can say that if NIPT is negative then no need for further test you rest assure that yes the fetus is normal, but if NIPT comes out to be positive then you further need to go for the diagnostic test that is the invasive test and then you can confirmly say whether the fetus is anomalous or not. So, what are the inferences we get from NIPT? Number 1 is the fetal RHDT, RHD typing right using the cell free fetal DNA to determine the fetal blood group status right and for this we need not go for invasive test like

amniocentesis. Number 2 is single gene disorder point mutation. These all can be detected from the genetic material right which are extracted from the mother circulation right and single gene disorder no there is the father has a mutation for that single gene disorder mother is normal in that case whether the baby is having the single gene disorder like in case of Marfan syndrome cystic fibrosis right.

Then Tay sach's disease BRCA 1 and 2 mutation right these all are as you know single gene point mutation and they can be detected in NIPT. Number 3 is fetal aneuploidy right chromosomal number defect, trisomy 21, Turner's syndrome, monosomy X which is monosomy X. So, all these can be detected from NIPT. So, NIPT is a very new concept it is very useful to detect the anomalous baby and it has a very high negative predictive value that means, a negative test is of importance and it confirmly says that the fetus is not anomalous it is healthy right. You can start doing NIPT from 10 weeks onwards right up till term right.

So, that was regarding the non-invasive prenatal diagnostic test done as a screening method right. So, we have discussed the prenatal diagnostic test, the screening test, the invasive test when to do and for whom to do not for all pregnant females. We need to first go for the screening mostly the first trimester screening for all pregnancies and then we need to assess you know whether they are low risk or high risk. For the high risk group we now go for further secondary diagnostic test that is the NIPT or we can directly go for the invasive diagnostic test to confirm the anomaly and if the fetus comes out to be anomalous then whether it is compatible to life or not you need to ascertain and if it is not compatible to life then you can go for termination of pregnancy right. So, that was regarding the prenatal diagnostic test and here today this is up till for today's class the references are taken from D.C.Dutta textbook of obstetrics, the Williams obstetrics at the James book on high risk pregnancy.

So, thank you all and I look forward to meet you all again in the next video.