DEPARTMENT OF GENOMICS AND MOLECULAR DIAGNOSTICS

Patient Name	**Mrs. SWEETI KUMARI**	**Visit ID**		**Collection Date**	**10-03-2024 04:34 PM**
Age / Gender	**32 Y / FEMALE**	**UHID**		**Registration Date**	**10-03-2024 04:28 PM**
Gestational age	**16.4 weeks**	**Fetus number**	**Single**		

NIPT

Referral reason

The marker screening is indicative of high risk for Trisomy 21 (1:90).Sample was referred for antenatal screening test to test for fetal aneuploidy.

Result and Interpretation

No Results .

NOTE : chromosomal aneuploidy is one of the possibility for low fetal fraction.(refer appendix)

- **Sample Received**: First
- **Result:** Fetal fraction is lower than required
- **Recommendation:** Repeat testing with fresh sample or Invasive Testing is highly recommended.

Ref: ACOG Practice Bulletin, Screening for Fetal Chromosomal Abnormalities. Vol 136, No. 4, 2020

Sample type	Estimated Fetal Fraction	cf DNA Quality	Sequencing Quality	Unique reads (M)
Maternal plasma (cfDNA)	1.76 (low)	Pass	Pass	10.68

Understanding the test Results: NIPT analysis can lead to one of the three following outcomes

A- **No Aneuploidy Detected:** Low probability of the fetus developing the specific chromosomal aneuploidy

B- **Aneuploidy Detected:** High probability of the fetus developing the specific chromosome aneuploidy.

Confirmatory testing via amniocentesis/CVS is recommended.

C- **No Results:** The maternal sample could not generate test results due to unavoidable reasons, therefore repeat sampling is recommended. Invasive testing is recommended if NO TEST RESULT is obtained subsequent to the repeat sampling.

About the Test

The cell-free DNA that was extracted from the peripheral blood of the mother was subjected to whole genome sequencing. The Next Generation Sequencing is performed using MGI platform and analyzed through the JINKE NIPT technology.

The test can detect aneuploidy across the entire fetal genome (23 pairs of chromosomes) and can interpret the results for Trisomy 13, Trisomy 18, and Trisomy 21, as well as sex chromosomes. This test has a detection accuracy of up to 99 percent for fetal

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chromosomal aneuploidy.

Recommendations

1. The above results need to be interpreted in the context of all clinical findings.
2. **Patients with negative NIPT results still require follow-up ultrasound examination and diagnostic testing is recommended incase of any scan anomalies**
3. **Invasive testing is recommended**

Test Limitations

*If the fetal fraction is lower than 3.5%, the accuracy of the test may be reduced. To ensure the accuracy of the results, we would recommend a re-sampling of the maternal blood one or two weeks later. If the fetal fraction is less than 7%, the detection power of fetal microdeletion/microduplication syndrome (< 5 Mb) is limited. We would recommend a more careful clinical observation or a higher coverage whole genome sequencing re-test.

1. The results of this test are for reference only, not for the final diagnosis. If the test result is high risk, genetic counseling and invasive prenatal diagnosis are needed. If a high risk of microdeletion/microduplication syndrome is detected, prenatal diagnosis is recommended to be combined with maternal chromosome analysis to exclude maternal influence. If the test result is low risk, the fetus has a low risk of developing the target disease of this screening. However, the possibility of other abnormalities cannot be excluded, and systematic ultrasound examinations and other prenatal examinations should be conducted
2. The results of this test include sex chromosome aneuploidies and other chromosomal aneuploidies. Compared with trisomy 21, trisomy 18 and trisomy 13, the incidence of these aneuploidies is lower in the population, and the data available is limited. Therefore, the possibility of false positive or false negative cannot be ruled out.
3. This method is not suitable for testing: Gestational age <12+0 weeks; Pregnant women with twins or multiple pregnancies; One partner has a definite chromosomal abnormality; Received allogeneic blood transfusion, transplantation and allogeneic cell therapy within 1 year; Fetal ultrasound result suggested that there were structural abnormalities and prenatal diagnosis was needed; A family history of genetic diseases or a high risk of genetic diseases in the fetus; Pregnancy with malignant tumor; Other conditions that the doctor considers may affect the accuracy of the results.
4. Abnormalities caused by the following factors cannot be detected in this test: structural abnormalities such as chimera and translocation in chromosomes; Chromosomal polyploidies (triploid, tetraploid, etc.); Balanced translocation, inversion and ring

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of chromosomes; Uniparental disomy (UPD); Single/polygenic diseases; Chromosomal regions with high duplication and fixation, such as the chromosomal abnormalities of the proximal centromere and telomere.

5. The sample tested is the cell free DNA in peripheral blood of pregnant women, which mainly from placental trophoblastic cells rather than direct fetal cells. Given the limitations of the current technical level of the medical tests and the differences among pregnant women, there may still be false positives or false negatives in rare cases, even if the testing staff has fulfilled job responsibilities and operational procedures.
6. The detection accuracy may be reduced to some extent for severely obese pregnant women (BMI >40) and conception through in-vitro fertilization-embryo transfer, and the test results are only for reference.
7. The patient should provide complete, accurate and detailed personal information. The center shall not be responsible for the interruption of testing services and inaccurate results caused by inaccurate information or other misleading factors provided by the patient.
8. The test results in this report are only responsible for the samples submitted for inspection.
9. The NIPT is a screening test; a low risk does not exclude the above evaluated disorders. It is not intended, either validated for diagnosis nor for use in pregnancies with more than two fetuses, mosaicism, partial chromosomal aneuploidy, translocations or maternal aneuploidy.
10. The NIPT is a screening test and the positive predictive value is not 100%. Hence confirmation of high-risk results is recommended by invasive testing

Important: On doing PNDT test, the undersigned hereby confirms that no sex chromosome information has been passed on to anyone in whatsoever manner.

Reference

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6. Chen, M., et al., Validation of fetal DNA fraction estimation and its application in noninvasive prenatal testing for aneuploidy detection in multiple pregnancies. Prenatal Diagnosis, 2019. 39(13): p. 1273-1282.
7. Fetal fraction and noninvasive prenatal testing: What clinicians need to know.Lisa Hui,Diana W. Bianchi, Prenatal Diagnosis 2020.
8. ACMG statement on noninvasive prenatal screening for fetal aneuploidy Anthony R. Gregg, S.J. Gross, R.G. Best, K.G. Monaghan, K. Bajaj, B.G. Skotko, B.H. Thompson and M.S. Watson. Genetics in Medicine 2013.

Appendix :

Understanding and Supporting document for NIPT -**NO RESULTS**

NIPT fails to return a result in **1–3% of women**. The most common cause for this is an insufficient cffDNA fraction, FF may be affected by many maternal factors, including BMI, maternal diseases or inflammatory states, race, and drugs or certain medications (such as Clexane), or exercise. When high maternal BMI and maternal diseases or inflammatory states are present, it is necessary to be aware that FF may be low.[1]

Chan et al. present results of a retrospective study showing that, as compared with the background population, women with 'no-call' or repeated low fetal fraction are at increased risk of chromosomal aneuploidies (6.5 versus 0.2%), pre-eclampsia (11 versus 1.5%) and gestational diabetes (23 versus 7.5%) [2]

Among women with noninformative results attributable to low FF, trisomy 18 and/or triploidy risk are sufficiently high to warrant offering additional assessments (e.g., ultrasound). **If the testing indication is ultrasound abnormality, amniocentesis and karyotype/microarray should be considered.**

The effect of IVF medications on the cell-free DNA (cfDNA) fetal fraction in non-invasive prenatal testing (NIPT) is an important consideration. IVF medications can potentially impact the cfDNA fetal fraction, which, in turn, can affect the accuracy and reliability of NIPT results. Here's how IVF medications may influence the cfDNA fetal fraction:

1. **Ovarian Stimulation Medications**: During the IVF process, women typically receive ovarian stimulation medications. These medications can lead to a higher maternal cfDNA fraction in the bloodstream, which may dilute the fetal fraction. This increase in maternal cfDNA can affect the accuracy of NIPT results, potentially making it more challenging to detect the fetal DNA.
2. **Timing of Medication Administration**: The timing of IVF medications is critical. If the timing is not optimal, it can affect the cfDNA fetal fraction. For example, medications given too early or too late in the IVF cycle may result in a less accurate representation of fetal DNA in the maternal bloodstream when NIPT is performed.
3. **Medication Side Effects**: Some IVF medications may have side effects that can influence cfDNA levels. For example, medications that affect blood clotting or platelet function may indirectly impact the amount of cfDNA in maternal circulation.[5]
4. **Patient-Specific Factors**: Each woman may respond differently to IVF medications, and individual factors, such as age, overall health, and underlying medical conditions, can also influence the cfDNA fetal fraction.

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In cases where IVF is involved, especially when dealing with high-risk pregnancies or specific concerns, prenatal genetic counselling and Invasive diagnosis is often recommended.

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***** End Of Report *****

Suggested clinical correlation & follow up

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