General information about positive NIPT results: Trisomy 21 (Down syndrome)

My patient's NIPT is positive for trisomy 21 (Down syndrome). What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result suggests the presence of an extra copy of chromosome 21. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 21 depends on many factors, including the patient's clinical and family history.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. Globally, professional medical societies recommend that all women with a positive screening result should have genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm the results.[1,2] Confirmation prior to birth can also help with pregnancy and neonatal management.

See below for more information about trisomy 21.

What is trisomy 21?

Trisomy 21 is a condition that is caused by an extra chromosome number 21 (three copies instead of two).

What are the features of trisomy 21?

Although some pregnancies with trisomy 21 end in pregnancy loss, trisomy 21 often can lead to live birth. Individuals with trisomy 21 have variable physical features and intellectual disability. Some common features of trisomy 21 include heart defects, duodenal atresia, low muscle tone, and differences in facial features. Some of these structural findings may be identified in second trimester ultrasound evaluation. In addition, cognitive impairment can range from mild to severe. People with Down syndrome have a higher risk for certain medical conditions, such as hearing problems, thyroid problems, childhood leukemia, and Alzheimer's disease. People with Down syndrome may require supervision throughout their lives. However, many people with Down syndrome are increasingly attending school and holding jobs. Many individuals with Down syndrome live into adulthood.

What is the prevalence of this condition?

Trisomy 21 is the most common chromosome anomaly, occurring in 1 in 700 to 800 live births. This condition usually happens by chance and is associated with increasing maternal age.

What testing could be considered?

Specialized genetic tests such as karyotyping, fluorescence *in situ* hybridization (FISH), quantitative polymerase chain reaction (qPCR), and microarray are available to confirm the presence of trisomy 21.

These confirmatory tests are generally performed on cells from chorionic villus sampling (CVS) or amniocentesis during pregnancy, on cord blood or peripheral blood sample after the baby is born, or on products of conception (POC) in the case of a miscarriage. The type of invasive procedure and diagnostic testing should take into account the underlying chromosome anomaly.[3,4]

Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 21, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 21

MedlinePlus Genetics medlineplus.gov/genetics/chromosome/21

National Down Syndrome Society (NDSS) ndss.org

Down's Syndrome Association (UK) downs-syndrome.org.uk

Deutsche Down-Syndrom InfoCenter (Germany) ds-infocenter.de

Down Syndrome Ireland downsyndrome.ie

European Down Syndrome Association edsa.eu

L'Associazione Italiana Persone Down (Italy) aipd.it/site

Association Romande Trisomie 21 (Switzerland) t21.ch

Down Syndrome Australia downsyndrome.org.au

Canadian Down Syndrome Society cdss.ca

References

1. Rose NC, Kaimal AJ, Dugoff L, et al. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. *Obstet Gynecol*. 2020;136(4):e48-e69.
2. Benn P, Borrell A, Chiu RW, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. *Prenat Diagn*. 2015;35(8):725-734.
3. Cherry AM, Akkari YM, Barr KM, et al. Diagnostic cytogenetic testing following positive noninvasive prenatal screening results: a clinical laboratory practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2017;19(8):845-850.
4. Van Opstal D, Srebniak MI. Cytogenetic confirmation of a positive NIPT result: evidence-based choice between chorionic villus sampling and amniocentesis depending on chromosome aberration. *Expert Rev Mol Diagn*. 2016;16(5):513-520.

Additional resources

Gardner RJM, Amor DJ. *Gardner and Sutherland's Chromosome Abnormalities and Genetic Counseling*. 5th ed. Oxford University Press; 2018.

Jones KL, Jones MC, del Campo M. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. W.B. Saunders Company; 2013.

Malvestiti F, Agrati C, Grimi B, et al. Interpreting mosaicism in chorionic villi: results of a monocentric series of 1001 mosaics in chorionic villi with follow-up amniocentesis. *Prenat Diagn*. 2015;35(11):1117-1127.

Pub. No. 1576-2020-056 QB9694