

General information about positive NIPT results: Trisomy 14

My patient's NIPT is positive for trisomy 14. What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result suggests the presence of an extra copy of chromosome 14. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 14 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 14.

What is trisomy 14?

Trisomy 14 is a condition that is caused by an extra chromosome number 14 (three copies instead of two).

What are the features of trisomy 14?

Most pregnancies with trisomy 14 will miscarry spontaneously. Full trisomy 14 has not been reported in live births and there are only a few reports of viability into the late first or second trimester. If a developing fetus has mosaic trisomy 14 (where some cells are normal and some cells have trisomy 14), there is an increased chance for the pregnancy to progress and possibly survive to term. However, liveborn infants with mosaic trisomy 14 are expected to have serious medical problems. Key features include: intellectual disability, growth restriction, dysmorphism, and organ system anomalies. In reported cases of prenatally diagnosed trisomy 14, the outcomes have ranged from normal to live births with clinical sequelae. The variability in clinical presentation is believed to be due to confined placental mosaicism (CPM; when trisomic cells are present in the placenta, but not in the fetus) or the degree of fetal mosaicism.

What is the prevalence of this condition?

Unknown, but rare. For this reason, positive predictive value (PPV) cannot be accurately calculated.

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 14. Uniparental disomy (UPD) analysis is performed by specialized testing, such as single nucleotide polymorphism (SNP) microarray, methylation testing, and short tandem repeat (STR) marker testing.

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 14, but a normal ultrasound cannot exclude this condition.

Special considerations

Chromosome 14 is an imprinted chromosome and UPD for chromosome 14 has specific consequences. Maternal UPD 14 is associated with a somewhat variable phenotype, including an increased risk of growth deficiency, intellectual disability, and dysmorphism. Paternal UPD 14 is associated with intellectual disability, dysmorphism, and a thoracic deformity that can lead to lethal respiratory failure in infancy. There may be an increased risk for certain recessive conditions if UPD is present.

The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients when there is discordance noted between NIPT results and the diagnostic testing.⁵

Resources for trisomy 14

MedlinePlus Genetics
medlineplus.gov/genetics/chromosome/14

Unique, The Rare Chromosome Disorder Support Group
rarechromo.org

References

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Additional resources

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