Study of Noonan syndrome in abortions of fetuses with increased nuchal translucency

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Introduction

Increased Nuchal Translucency (NT) in the first trimester is associated with higher risk of aneuploidy, congenital heart disease, and other structural anomalies or genetic syndromes. The association between increased NT and Noonan syndrome has been reported many times. It is the most common single gene anomaly in fetuses with increased NT, with an incidence of 7-10%.
Therefore, there is growing evidence that the management of these pregnancies should include the genetic study of Noonan syndrome.

Objective

To report the prevalence of Noonan syndrome in euploid fetuses with increased nuchal translucency thickness in the first trimester of pregnancy which had a miscarriage or termination of pregnancy.

Methods

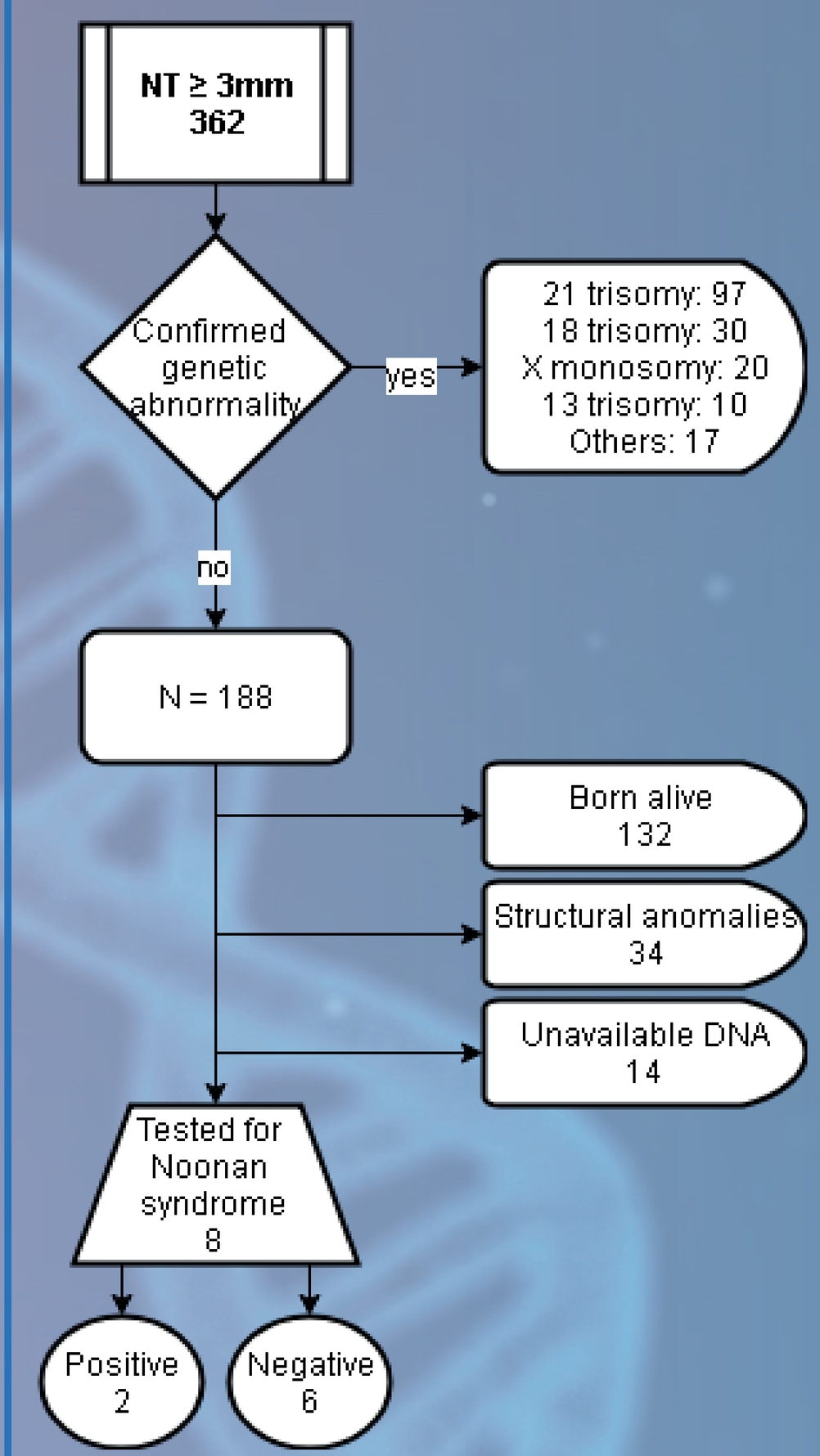
A retrospective cohort study including singleton pregnancies with a first trimester NT measurement of 3 mm or higher that did not have a genetic abnormality diagnosis and had a miscarriage or pregnancy termination in our centre. The selected pregnancies were tested for PNPT11, SOS1, RAF1, KRAS and RIT1 mutations.

Results

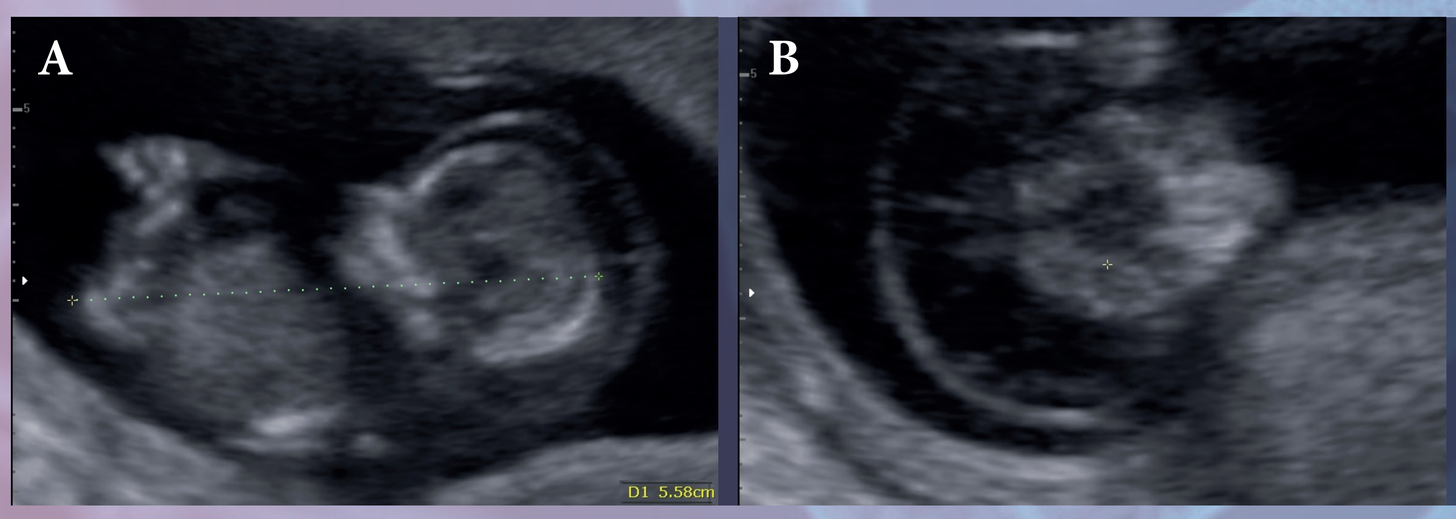
A total of 362 fetuses had a NT measurement of 3 mm or higher. Of these, 171 had been diagnosed with a genetic abnormality. Among the 188 fetuses with a normal or unknown karyotype, 132 were born alive, 34 had structural abnormalities unrelated to Noonan syndrome and in 14 DNA was unavailable. Finally 8 patients had the Noonan syndrome gene sequencing panel done and 2 (25%) of them tested positive for Noonan syndrome, one had a PNPT11 mutation and the other RIT1 mutation.

Conclusion

Increased NT is associated with a significant risk of Noonan syndrome. Testing for Noonan syndrome should be considered in fetuses with an increased NT and normal karyotype and/or array-CGH.



Flow chart showing included and excluded pregnancies.



Fetus at 12.6 weeks of gestation affected by Noonan Syndrome (RIT1 mutation).
A. Mid-sagittal plane.
B. Axial plane showing cervical region.

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