

Time to update our counselling on the association of fetal structural abnormalities with aneuploidy

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Short Title: Fetal anomalies and aneuploidy

Keywords: Duodenal atresia, cleft lip and palate, aneuploidies, chromosomal abnormalities, structural anomalies

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/uog.21934

Introduction:

Traditionally, both duodenal atresia (DA) (usually diagnosed after 25 weeks) and cleft lip ± palate (CL/P) (usually diagnosed in the second trimester) are associated with a higher risk of trisomy (trisomy 21 in the case of DA, and trisomies 13 and 18 in the case of CL/P). In the era of first trimester screening, however, most fetuses with trisomy are diagnosed, and often undergo termination, in the first trimester, prior to any ultrasound diagnosis of congenital anomalies. We hypothesized that this change in practice would lead to a less strong association between the later diagnosis of these anatomical abnormalities and the presence of trisomy. It therefore would be prudent to revisit these associations in order to adjust our counselling accordingly.

We performed a retrospective review of all cases of DA and CL/P encountered in a tertiary Fetal Medicine centre over the last 20 years, with the majority being in the last 10 years, and the prevalence of associated aneuploidies in these cases.

Duodenal atresia:

DA is reported to be associated with trisomy 21 in up to 44% of cases¹⁻³. In our cohort, 31 patients had prenatal ultrasound findings suggestive of DA [Figure 1], with the earliest diagnosis at 19 weeks' gestation. Of those, 4 patients were lost to follow-up. Only 4 (15%) of the remaining 27 cases were diagnosed with trisomy 21, and 1 with mosaic trisomy 21. Three of these cases with trisomy 21 had associated anomalies, all of which were cardiac in origin. 3 patients in this cohort did not undergo first trimester screening, and none of these cases had trisomy 21. Those who had a confirmed diagnosis of T21 all underwent screening, and all but one had a low trisomy 21 risk. Therefore, the association between isolated DA and trisomy 21 in the current era is less than originally reported in the old literature.

Cleft lip ± palate:

Previous literature has demonstrated that the incidence of aneuploidy is up to 35% in fetuses diagnosed with CL/P in the second trimester [Figure 2]. However, in the absence of other structural anomalies, there was no association with an abnormal karyotype^{4,5}. Conversely, the incidence of aneuploidy was 27-32%⁴, with reports as high as 58%⁵, when other anomalies are present.

We analysed 307 cases of ultrasound diagnosed CL/P, of which 97 were lost to follow-up. Of the remaining 210 cases, only 15 (7%) were diagnosed with aneuploidy (majority trisomy 13), and all 15 were associated with other ultrasound anomalies. Of the initial 307 cases, 72 (23%) had additional anomalies detected on ultrasound. Excluding the cases who did not undergo genetic testing, 24% (n=15) of those with anomalies had aneuploidies. This is less than the previously reported associations. Cardiac anomalies were the most common of the anomalies seen (n=35, 49%), followed by brain abnormalities (n=30, 42%). Interestingly, a large percentage of babies with aneuploidies also had cardiac anomalies (n=12, 80%).

18 patients in our cohort did not undergo first trimester screening. A third of these cases were lost to follow up (n=6), but none of the remaining 12 patients had aneuploidies. Of the 15 cases with confirmed aneuploidies, 3 cases did not report on first trimester screening, but the remainder all underwent screening. Gestational age at diagnosis were mostly following the second trimester anomaly scans, with 2 cases diagnosed in the third trimester, and 2 diagnosed during the first trimester scan.

The UK National Screening Committee formally recommended routine first trimester screening for trisomies 18 and 13 in 2014; prior to this screening only for trisomy 21 had been recommended. The previous policy was to screen for trisomies 18 and 13 as part of the second trimester fetal anomaly scan. However, in our centre, screening for trisomies 18 and 13 was included in the implementation of the first trimester combined test before this change in the national recommendations. Recently, a large screening study which included 100,997 singleton pregnancies have reported that approximately one third of cases of CL/P were diagnosed in the first trimester, while two thirds were diagnosed in the second trimester.⁶ As expected, none of the cases of duodenal atresia was diagnosed in the first trimester and almost 90% were diagnosed in the third trimester.⁶

Conclusion:

Our data show that the association between DA, CL/P and trisomy is now weaker since the advent of first trimester screening for trisomy. It is possible that there has been a similar effect on the relationship between other anomalies and aneuploidies. This should be reflected in updated counselling of parents in whom these ultrasound anomalies are diagnosed.

Accepted Article

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Figure Legends:

Figure 1: 2D ultrasound image demonstrating the characteristic “double bubble” sign associated with duodenal atresia

Figure 2: Coronal view of the fetal face demonstrating a large left sided cleft lip extending to the midline, with the defect measuring 4.4mm



