Outcome Following Autosomal Monosomy and Multiple Aneuploidy
Results by Noninvasive Prenatal Screening

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Introduction

- A recent study of cytogenetic analysis following spontaneous miscarriage showed that 5% of samples were affected with a multiple aneuploidy.\(^1\)
- An estimated 0.16% of trisomy 21 cases involve a double aneuploidy with either XXX, XXY, XY or MX. The combination of Down syndrome and Klinefelter syndrome is the most common.\(^2\)
- Full autosomal monosomies are not generally compatible with life; however, partial and mosaic forms of autosomal monosomy have been reported in liveborns.
- This study evaluates outcomes of clinical laboratory noninvasive prenatal screening (NIPS) samples from singleton pregnancies receiving multiple aneuploidy and/or autosomal monosomy results.

Method

- Database query for all singleton NIPS samples during the study period with one of the following results:
  - Single autosomal monosomy
  - Multiple aneuploidy with aneuploidy detected (AD) and/or aneuploidy suspected (AS) for chromosomes 21, 18, 13, X and Y
- Outcome information was requested for all cases via:
  - Fax requests
  - Outgoing and incoming phone calls
- Data on 138 samples was reviewed
- Results were classified into one of three categories

Case Examples

Autosomal Monosomy
- Clinical hx: 24 y.o. with Dandy Walker malformation on ultrasound
- NIPS result: full/partial monosomy for chromosome 13
- Prenatal dx: declined
- Outcome: term delivery
- Postnatal array: c/w 9.3Mb deletion on chromosome 13q

Multiple Aneuploidy
- Clinical hx: 33 y.o. with echogenic intracardiac focus and shortened long bones on ultrasound
- NIPS result: aneuploidy detected for chromosomes 21 and 18
- Prenatal dx: declined
- Outcome: postnatal fetal karyotype c/w 47, +21; placental analysis c/w mosaic trisomy 18

Results by Noninvasive Prenatal Screening

Results were classified into one of three categories:
- Single autosomal monosomy
- Single Trisomy with Sex Chromosome Abnormality
- Multiple Aneuploidy

<table>
<thead>
<tr>
<th>Result Classification</th>
<th>n=138</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Autosomal Monosomy</td>
<td>25.4%</td>
</tr>
<tr>
<td>Single Trisomy with Sex Chromosome Abnormality</td>
<td>26.8%</td>
</tr>
<tr>
<td>Multiple Aneuploidy</td>
<td>47.8%</td>
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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Concordance</th>
<th>Single Autosomal Monosomy</th>
<th>Single Trisomy with Sex Chromosome Abnormality</th>
<th>Multiple Aneuploidy</th>
<th>Total Cohort</th>
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<td>1</td>
<td>5</td>
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<tr>
<td>Partially Concordant(^a)</td>
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<td>3</td>
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<td>Discordant</td>
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<td>10</td>
<td>14</td>
<td>44</td>
<td></td>
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<tr>
<td>Other(^a)</td>
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<td>6</td>
<td>9</td>
<td>22</td>
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<tr>
<td>Outcome Unknown</td>
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<td>7</td>
<td>10</td>
<td>42</td>
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<tr>
<td>Outcome Unknown, EDD Not Passed(^a)</td>
<td>12</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>66</td>
<td>35</td>
<td>37</td>
<td>138</td>
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</tbody>
</table>

\(^a\) Concordance confirmed for one aneuploidy
\(^a\) Other outcomes include SAB/TOP/IUFD, maternal conditions and other reported fetal karyotype anomalies
\(^a\) EDD not passed as of data collection


Results

<table>
<thead>
<tr>
<th>Sample Demographics by Result Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>66</td>
</tr>
</tbody>
</table>

Mean Maternal Age (years) 34.4 (19–46) 37.3 (24–47) 35.3 (23–44) 35.4 (19–47)
Mean Gestational Age (weeks) 14.8 (10–32) 12.0 (10–25) 14.0 (10–34) 13 (10–34)
Outcomes Received 29 (43.9%) 25 (71.4%) 26 (70.3%) 81 (58.7%)

1 Includes AD and AS results
2 EDD not passed at time of data collection

Summary of Findings

► Overall, full or partial concordance was confirmed in 15 (10.9%) cases
► An additional 13 (9.4%) cases were explained by other biological etiologies, including maternal malignancy (7, 5.1%), maternal karyotype anomalies (1, 0.7%) or other fetal karyotype anomalies (5, 3.6%)
► Some autosomal monosomies were explained by abnormalities in one of the reference chromosomes used to analyze test chromosomes

Conclusions

► Although in most cases, abnormal NIPS results relate to a single trisomy, other results may be reported.
► We anticipate that a portion of multiple aneuploidy and autosomal monosomy findings reflect the fetal karyotype while some may be explained by other etiologies, such as other maternal/fetal chromosomal aberrations, maternal disease, mosaicism or co-twin demise.
► Continued evaluation of outcomes for complex NIPS results is warranted to better understand the biological reasons for such results

References