Risk factors for monozygotic twinning in IVF: a multicenter, cohort study


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Disclosures

- Nothing to disclose
Objectives

- Background on monozygotic twinning (MZT)
- Preliminary results
- Future study plans
- Questions
Background

Identical (Monozygotic)
- Sperm
- Egg
- (Shared placenta)

Fraternal (Dizygotic)
- (Separate placenta)
Background
Background

- Monozygotic (MZ) twins carry a significantly higher risk of perinatal morbidity and mortality than singleton and dizygotic twins\(^1,2\)
- Increased risk of premature delivery\(^1\)
- Growth discordance\(^3\)
- Developmental anomalies\(^4\)
- Mortality\(^1\)
Background

- Incidence of MZ twinning (MZT) is greatly increased amongst IVF patients compared to the general population (0.7-13% vs. 0.45%, respectively)
- Reason for this remains unclear\textsuperscript{5,6}
Background

- Prolonged embryo culture, appears to be a risk factor\(^6\)
- Studies have also hypothesized that media characteristics—such as glucose\(^7\) or glutathione levels—may affect MZT rates.
- Zona Pellucida micromanipulation may be involved
- Others have suggested that the high incidence of MZT in infertility patients is conditioned by hereditary factors\(^8\)
Study Objective

- Create a large, multicenter database to include data on monozygotic twinning in IVF
- To investigate risk factors for MZT
Methods

- Using an electronic medical record system (eIVF, PracticeHwy), clinical pregnancy data (confirmation of a gestational sac(s) and presence of a fetal pole with a heartbeat(s) on ultrasound)

- Data from 10 large IVF clinics in the U.S from January 1st 2000 to January 31st 2017 were retrospectively reviewed.

- Both fresh and thaw cycles were included
Methods

- MZT: when the number of fetal poles with cardiac activity seen and recorded exceeded the number of embryos transferred

- A binary logistic regression was performed to ascertain risk factors for MZT within our cohort
Results

- >124,000 clinical pregnancies identified in the database
- 61,924 clinical pregnancies met criteria for modeling
- 50,215 pregnancies resulted from fresh transfers
- 11,709 pregnancies resulting from thaw transfers
<table>
<thead>
<tr>
<th>Cohort characteristics</th>
<th>(n= 61,924)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Fresh</th>
<th>Frozen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at cycle start</td>
<td>36.14 +/- 5.04</td>
<td>37.48 +/- 5.8</td>
<td>36.39 +/- 5.2</td>
</tr>
<tr>
<td>Transfer Day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 days</td>
<td>28240 (45.6%)</td>
<td>1022 (1.7%)</td>
<td>29262 (47.3%)</td>
</tr>
<tr>
<td>4-7 days</td>
<td>21975 (35.5%)</td>
<td>10687 (17.3%)</td>
<td>32662 (52.7%)</td>
</tr>
<tr>
<td>PGD performed</td>
<td>2140 (3.5%)</td>
<td>501 (0.8%)</td>
<td>2641 (4.3%)</td>
</tr>
<tr>
<td>Embryos transferred</td>
<td>2.13 +/- 1.06</td>
<td>0.93 +/- 1.84</td>
<td>1.9 +/- 1.12</td>
</tr>
<tr>
<td>IVF performed</td>
<td>25201 (40.7%)</td>
<td>0</td>
<td>25201 (40.7%)</td>
</tr>
<tr>
<td>ICSI performed</td>
<td>28566 (46.1%)</td>
<td>0</td>
<td>28566 (46.1%)</td>
</tr>
<tr>
<td>Assisted hatching performed</td>
<td>9573 (15.5%)</td>
<td>0</td>
<td>9573 (15.5%)</td>
</tr>
</tbody>
</table>
Results

- 352 cycles (0.57%) resulted in MZ twins
- 198 in the fresh cycle group
- 154 in the thaw cycle group
### Monozygotic Twin Cohort Characteristics

(n=352, 0.57%)

<table>
<thead>
<tr>
<th></th>
<th>MZT</th>
<th>Non-MZT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at cycle start</strong></td>
<td>35.8 +/- 5.76</td>
<td>36.4 +/- 5.22</td>
<td>36.39 +/- 5.2</td>
</tr>
<tr>
<td><strong>Transfer Day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 days</td>
<td>49 (0.1%)</td>
<td>29213 (47.2%)</td>
<td>29262 (47.2%)</td>
</tr>
<tr>
<td>4-7 days</td>
<td>303 (0.5%)</td>
<td>32359 (52.3%)</td>
<td>32662 (52.7%)</td>
</tr>
<tr>
<td><strong>PGD performed</strong></td>
<td>28 (0.04%)</td>
<td>2613 (4.2%)</td>
<td>2641 (4.3%)</td>
</tr>
<tr>
<td><strong>Embryos transferred</strong></td>
<td>1.25 +/- 0.7</td>
<td>1.91 +/- 1.1</td>
<td>1.9 +/- 1.12</td>
</tr>
<tr>
<td><strong>Any embryo biopsy</strong></td>
<td>133 (0.2%)</td>
<td>30062 (48.2%)</td>
<td>30195 (48.8%)</td>
</tr>
</tbody>
</table>
Table 1. Risk Factors for MZT events among 61,920 IVF cycles from Jan 2000 through Dec 2016. Adjusted odds ratios and p-values from multivariable logistic regression.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at cycle start</td>
<td>0.99 (0.97-1.00)</td>
<td>0.15</td>
</tr>
<tr>
<td>Transfer Day</td>
<td>1.44 (1.26-1.60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thaw cycle</td>
<td>1.94 (1.37-2.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Assisted hatching</td>
<td>0.97 (0.93-1.02)</td>
<td>0.27</td>
</tr>
<tr>
<td>ICSI</td>
<td>0.99 (0.97-1.01)</td>
<td>0.38</td>
</tr>
<tr>
<td>PGS</td>
<td>1.39 (0.91-2.11)</td>
<td>0.13</td>
</tr>
<tr>
<td>Number of oocytes retrieved</td>
<td>1.03 (1.02-1.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number embryos transferred</td>
<td>0.66 (0.57-0.77)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Conclusions (Preliminary)

- We have validated the hypothesis that prolonged embryo culture is a major risk factor for MZT.
- For each additional day in culture the OR for MZT increases by 1.4.
- Thaw cycles appear to be twice as likely to result in MZT.
Future Studies

- Further investigate potential risk factors behind the increase in likelihood of MZT
- Investigate our clustering theory across all clinics independently
- Identify laboratory or clinical changes which may increase the risk of monozygotic clinic
References


Acknowledgements

- Boston IVF faculty and Staff
- Department of OBGYN at Tufts Medical Center
- New England Fertility Society/eIVF
- Irvine Scientific
Thank you