Risk of adverse obstetric outcome after early pregnancy complications

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SIGEP Rotterdam 2009
FIRST TRIMESTER COMPLICATIONS

- First trimester events and complications are common
- Distressing for the patient
- Fear for outcome → miscarriage?

- Clinician:
  - Confirm fetal viability
  - To reassure and to support the couple
FIRST TRIMESTER COMPLICATIONS

Are these women, who had a first trimester complication, at risk of obstetric and perinatal complications in the subsequent or ongoing pregnancy?
LITERATURE REVIEW

**Placental related disorders**
- Preeclampsia
- Placental abruption
- SGA p<10\(^{th}\) and p<5\(^{th}\)

**Obstetric outcome**
- PPROM
- Preterm delivery <37 weeks
- Preterm delivery <34 weeks

**Perinatal Outcome**
- Congenital malformation
- 5 min Apgar Score < 7
- Fetal and neonatal death

**1\(^{st}\) trimester events**
- Miscarriage
- Recurrent miscarriage
- Termination of pregnancy

**1\(^{st}\) trimester complications**
- Threatened miscarriage
- Intrauterine hematoma
- CRL- discrepancy
- Vanishing twin
- Hyperemesis gravidarum
LITERATURE REVIEW

- Pubmed 1980-2009
- Using combinations of MeSH terms for each specific association
- Using ‘umbrella’ approach (pregnancy outcome, etiology, risk factors)
- Reference lists were searched by hand

- Excluded: non-English, without a control group or with an inappropriate control group, poorly defined obstetric and perinatal outcome

- Number of appropriate studies found: 57
- Mostly retrospective population-based, cohort and case-control studies
Predicting adverse obstetric outcome after early pregnancy events and complications: a review

R.H.F. van Oppenraaij¹, E. Jauniaux², O.B. Christiansen³, J.A. Horcajadas⁴, R.G. Farquharson⁵ and N. Exalto¹,⁶, on behalf of the ESHRE Special Interest Group for Early Pregnancy (SIGEP)

- Odds Ratio (OR) and Standard Error (SE) were used for analysis
- Meta-analyse: Random effects model
- MIX 1.7¹,²

¹ Bax et al., 2006; ² Bax et al., 2008
PREVIOUS MISCARRIAGE(S)

Risk of adverse obstetric outcome in the subsequent pregnancy

- At least controlled for: parity and age

- Single miscarriage - 20 studies
- Two or more miscarriages - 14 studies
- Three or more miscarriages - 5 studies
### SINGLE PREVIOUS MISCARRIAGE & PREECLAMPSIA

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Year</th>
<th>Weight (%)</th>
<th>Association measure with 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhattacharay</td>
<td>2008</td>
<td>32,00%</td>
<td>1,1 (0,96 to 1,26)</td>
</tr>
<tr>
<td>Dempsey</td>
<td>2003</td>
<td>4,00%</td>
<td>0,8 (0,33 to 1,94)</td>
</tr>
<tr>
<td>Eras</td>
<td>2000</td>
<td>1,00%</td>
<td>0,23 (0,02 to 2,75)</td>
</tr>
<tr>
<td>Eskenazi</td>
<td>1991</td>
<td>2,00%</td>
<td>0,89 (0,2 to 3,93)</td>
</tr>
<tr>
<td>Seidman</td>
<td>1989</td>
<td>10,00%</td>
<td>0,46 (0,27 to 0,77)</td>
</tr>
<tr>
<td>Thom</td>
<td>1992</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Trogstad</td>
<td>2008</td>
<td>24,00%</td>
<td>0,93 (0,77 to 1,13)</td>
</tr>
<tr>
<td>META-ANALYSIS</td>
<td></td>
<td>28,00%</td>
<td>0,98 (0,82 to 1,18)</td>
</tr>
</tbody>
</table>

Studies controlled for: age, BMI, parity and smoking
PREVIOUS MISCARRIAGE(S) & OBSTETRIC OUTCOME

Odds Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>One</th>
<th>Two</th>
<th>Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPROM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm &lt;37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm &lt;34</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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PREVIOUS MISCARRIAGE(S) & PERINATAL OUTCOME

Odds Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>One</th>
<th>Two</th>
<th>Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cong. malformation</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Fetal death</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal death</td>
<td>4.0</td>
<td>2.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>
MISCARRIAGE(S) & ADVERSE OUTCOME: ETIOLOGY

- **Short interpregnancy interval**
  - Inadequate time to recover results in depletion of maternal nutrients\(^1\)
  - Previous term delivery → increased risk of preterm delivery\(^2\)
  - Stratification of interpregnancy interval after miscarriage: no association\(^3\)

- **Treatment modality**
  - MIST-trial: no difference in infection and live birth rate\(^4,5\)
  - No good studies on treatment modality and specific adverse obstetric outcome

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\(^1\) Winkvist, 1992; \(^2\) Conde-Agudelo, 2006; \(^3\) Buchmayer, 2004; \(^4\) Smith, 2009; \(^5\) Trinder, 2006
MISCARRIAGE(S) & ADVERSE OUTCOME: ETIOLOGY

- Shared risk factors for recurrent miscarriage and obstetric complications
  - Thrombophilia disorders
  - Maternal immunological or hormonal abnormalities
  - Chromosomal abnormalities
  - Infection
  - Incompetent cervix
  - Uterine abnormalities

- Only one study made a differentiation in underlying causes\(^1\)
  - Too small to permit correct analysis

1 Jivraj, 2001
PREVIOUS TERMINATION(S) OF PREGNANCY

Risk of adverse obstetric outcome in the subsequent pregnancy

At least controlled for: parity, age, ethnicity, socio-economics, BMI and smoking

- Single TOP - 18 studies
- Two or more TOP - 17 studies
PREVIOUS TOP & PLACENTAL DISORDERS

- **Odds Ratio**

  - **Preeclampsia**
  - **Placenta abruption**
  - **SGA**

  - **One**
  - **Two**
PREVIOUS TOP & OBSTETRIC OUTCOME

Odds Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>One</th>
<th>Two</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPROM</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Preterm &lt;37</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Preterm &lt;34</td>
<td>5.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>
PREVIOUS TOP & PERINATAL OUTCOME

Odds Ratio

- Cong. malformation
- Fetal death
- Neonatal death

One
Two
TOP & ADVERSE OUTCOME: ETIOLOGY

- Short or long interpregnancy interval
  - Stratification of interpregnancy interval after TOP\(^1\): no association

- Treatment modality
  - No good studies

- Timing of TOP
  - No good studies

- Complicated TOP
  - cervical damage, infection, tissue retention, adhesions

\(^1\) Zhou, 2003;
THREATENED MISCARRIAGE

- Incidence 14-20%\(^1,2\)
- ~50% miscarriage\(^1-3\) \(\rightarrow\) confirmation of viability \(\rightarrow\) 2-14% miscarriage\(^3-5\)

Risk of adverse obstetric outcome in the ongoing pregnancy

- At least controlled for age and parity in studies of blood loss
  - (Light) blood loss - 9 studies
  - Heavy blood loss - 3 studies
  - Intrauterine hematoma - 4 studies

\(^1\) Everett 1997; \(^2\) Weiss et al., 2004; \(^3\) Wijesiriwardana et al., 2006; \(^4\) Johns et al., 2006; \(^5\) Schauburger et al., 2005
THREATENED MISCARRIAGE & PLACENTAL DISORDERS

- Light Hematoma
- Heavy Hematoma

Odds Ratio

- Preeclampsia
- Placental Abruption
- SGA

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THREATENED MISCARRIAGE & PERINATAL OUTCOME

![Graph showing odds ratios for different outcomes: Cong. malformation, Fetal death, Neonatal death. The graph compares Blood loss (green) and Hematoma (black).]
THREATENED MISCARRIAGE & ADVERSE OUTCOME: ETIOLOGY

- Could be the result of an impaired placentation
  - At risk for adverse obstetric outcome
  - Congenital malformation

- Could cause disruption of the chorionic-amniotic plane\textsuperscript{1,2,3}
  - Rupture of membrane
  - Chronic inflammatory reaction $\rightarrow$ stimulate contractions
  - Nidus for infection

- Could lead to placental insufficiency secondary to scarring\textsuperscript{4}
  - SGA, preeclampsia and placental abruption

\textsuperscript{1} Johns and Jauniaux 2006; \textsuperscript{2} Weiss, 2003; \textsuperscript{3} Wijesiriwardana, 2006; \textsuperscript{4} Williams, 1991
CRL DISCREPANCY

- If measured Crown-Rump Length (CRL) is smaller than expected (2-6 days)
  - Associated with higher risk of miscarriage¹
  - Associated with aneuploidy²-⁶

¹ Reljic 2001; ² Kuhn et al., 1995; ³ Schermer et al., 1997; ⁴ Bahado-Sing et al., 1997; ⁵ Falcon et al., 2005; ⁶ Goldstein et al., 1996;
## CRL DISCREPANCY & OUTCOME

<table>
<thead>
<tr>
<th>Obstetric outcome</th>
<th>CRL discrepancy</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>PPROM</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Preterm delivery &lt;37 weeks</td>
<td>1.0 (0.7-1.5)</td>
<td>1</td>
</tr>
<tr>
<td>Very preterm delivery &lt;34 weeks</td>
<td>2.0 (1.1-4.0)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrauterine growth restriction &lt;5th</td>
<td>2.8 (1.9-4.3)</td>
<td>1</td>
</tr>
<tr>
<td>Small for gestational age &lt;10th</td>
<td>1.1 (1.0-1.2)</td>
<td>1</td>
</tr>
<tr>
<td>Congenital malformation</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Low 5-minute Apgar score</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Intrauterine fetal death</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>0.8 (0.2-3.3)</td>
<td>1</td>
</tr>
</tbody>
</table>

Data are reported as Odds Ratio (OR) with 95% Confidence Interval.
VANISHING TWIN PHENOMENON

Spontaneous reduction of a multiple pregnancy

Incidence 10-30%\textsuperscript{1-3}

IVF-population

\textsuperscript{1} Dickey et al., 2002; \textsuperscript{2} Landy and Keith 1998; \textsuperscript{3} Pinborg et al., 2005

Picture: The Gloaming
Survivors of vanishing twin IVF pregnancies, which were spontaneously reduced from twin to singleton pregnancies, were compared with singleton IVF pregnancies.

- Vanishing twin - 7 studies

- Only one study controlled for: age, ICSI vs. IVF and parity¹

¹ Pinborg et al., 2005
VANISHING TWIN & PLACENTAL DISORDERS

Survivor

Odds Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>4.5</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>3.2</td>
</tr>
<tr>
<td>SGA</td>
<td>2.0</td>
</tr>
</tbody>
</table>

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VANISHING TWIN & OBSTETRIC OUTCOME

![Graph showing odds ratios for different obstetric outcomes](image)

- **Survivor**

  - **Odds Ratio**
  - **PPROM**
  - **Preterm <37**
  - **Preterm <34**
VANISHING TWIN & PERINATAL OUTCOME

Odds Ratio

Cong. Malformation  |  Fetal death  |  Neonatal death

Survivor
VANISHING TWIN & ADVERSE OUTCOME: ETIOLOGY

- **Implantation crowding**
  - Could result in unfavorable implantation site\(^1\)

- **Presence of products segregated after the vanishing twin\(^2\)**
  - Could result in chronic inflammatory reaction

- **Vanishing twin could result in blood loss**
  - Independent risk factor

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\(^1\) Depp, 1996; \(^2\) Pinborg, 2007;
HYPEREMESIS GRAVIDARUM

- Incidence 0.3-1.5%
- Exact etiology unknown; therefore treatment remains symptomatic
- Decreased risk of miscarriage OR 0.3, (95% CI 0.2-0.3)¹

- Hyperemesis gravidarum - 5 studies
  - Two studies controlled for confounders²

¹ Maconochie et al., 2007; ² Dodds et al., 2006
HYPEREMESIS GRAVIDARUM & OBSTETRIC OUTCOME

Odds Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA</td>
<td>1.0</td>
</tr>
<tr>
<td>Preterm &lt;37</td>
<td>1.0</td>
</tr>
</tbody>
</table>

HG

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HYPEREMESIS GRAVIDARUM & PERINATAL OUTCOME

Odds Ratio

- Cong. Malformation
- Fetal death
- Neonatal death

HG
CONCLUSIONS

- Early pregnancy complications are independent risk factors for adverse obstetric outcome in the subsequent or ongoing pregnancy.

- The found increased risks are related to the recurrence and/or severity of the 1st trimester complication.
CLINICAL IMPLICATIONS

- Clinicians have to be vigilant

- Could lead to better risk evaluation to identify women at risk

- Questionable whether this knowledge could prevent obstetric complications to occur

- But possibly, by intensification of care the anticipated detrimental effects can be avoided or reduced
ACKNOWLEDGEMENTS

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R. Farquharson

Rigshospitalet University Hospital, Copenhagen
O.B. Christiansen

Instituto Valenciano de Infertilidad Foundation, Valencia
Dr. J. Horcajadas

Institute for Women’s Health, Royal Free and University College Medical School, London
Prof. Dr. E.R. Jauniaux
## Table I: Early pregnancy events and complications as risk factors for adverse obstetric outcome in the subsequent pregnancy.

<table>
<thead>
<tr>
<th>Obstetric outcome</th>
<th>Previous miscarriage</th>
<th>Recurrent miscarriage</th>
<th>Termionation of pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One</td>
<td>Two or more</td>
<td>Three or more</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIH</td>
<td>1.2 (0.6-2.3)</td>
<td>2.2 (0.5-7.2)</td>
<td>1.0 (0.6-1.8)</td>
</tr>
<tr>
<td>PF</td>
<td>0.9 (0.8-1.1)</td>
<td>1.0 (0.9-1.1)</td>
<td>1.1 (0.6-2.0)</td>
</tr>
<tr>
<td>Placental Abruption</td>
<td>1.1 (0.8-1.7)</td>
<td>1.5 (1.1-1.7)</td>
<td>1.2 (0.4-3.1)</td>
</tr>
<tr>
<td>Placenta Previa</td>
<td>1.7 (0.9-3.2)</td>
<td>1.7 (1.3-2.3)</td>
<td>6.0 (1.6-22.2)</td>
</tr>
<tr>
<td>PPROM</td>
<td>1.3 (1.0-1.8)</td>
<td>1.6 (1.1-2.1)</td>
<td>2.1 (1.5-2.9)</td>
</tr>
<tr>
<td>Preterm &lt;37 weeks</td>
<td>1.3 (1.2-1.4)</td>
<td>1.9 (1.7-2.2)</td>
<td>2.4 (1.8-3.4)</td>
</tr>
<tr>
<td>Preterm &lt;34 weeks</td>
<td>1.5 (1.3-1.8)</td>
<td>2.1 (2.2-3.3)</td>
<td>3.8 (1.6-9.0)</td>
</tr>
<tr>
<td>Perinatal outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGA</td>
<td>1.0 (1.0-1.1)</td>
<td>1.3 (1.1-1.5)</td>
<td>1.3 (0.9-1.7)</td>
</tr>
<tr>
<td>LBW &lt;2500g</td>
<td>1.2 (1.0-1.3)</td>
<td>1.5 (0.9-2.5)</td>
<td>2.0 (1.4-2.7)</td>
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<tr>
<td>LBW &lt;1500g</td>
<td>no data</td>
<td>no data</td>
<td>no data</td>
</tr>
<tr>
<td>Cong. malformation</td>
<td>1.3 (1.0-1.7)</td>
<td>no data</td>
<td>1.8 (1.1-3.0)</td>
</tr>
<tr>
<td>5 min A &amp;S &lt;7</td>
<td>1.0 (1.0-1.2)</td>
<td>1.0 (0.6-1.4)</td>
<td>0.6 (0.3-1.6)</td>
</tr>
<tr>
<td>Fetal death</td>
<td>1.6 (0.9-2.8)</td>
<td>no data</td>
<td>no data</td>
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<tr>
<td>Perinatal death</td>
<td>2.1 (1.0-3.9)</td>
<td>1.2 (0.9-1.4)</td>
<td>no data</td>
</tr>
</tbody>
</table>

Data are reported as Odds Ratio (OR) with 95% Confidence Interval (CI)
# FIRST TRIMESTER COMPLICATION

Table II: Early pregnancy events and complications as risk factors for adverse obstetric outcome in the ongoing pregnancy.

<table>
<thead>
<tr>
<th>Obstetric outcome</th>
<th>Threatened miscarriage</th>
<th>N</th>
<th>Intrauterine haematoma</th>
<th>N</th>
<th>CRL discrepancy</th>
<th>N</th>
<th>Vanishing twin</th>
<th>N</th>
<th>Hyperemesis gravidarum</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage</td>
<td>1.8 (1.7-1.0)</td>
<td>2</td>
<td>no data</td>
<td>0</td>
<td>no data</td>
<td>0</td>
<td>0.9 (0.6-1.3)</td>
<td>1</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>PIH</td>
<td>1.4 (1.1-1.8)</td>
<td>1</td>
<td>2.1 (1.5-2.9)</td>
<td>1</td>
<td>1.0 (0.8-1.2)</td>
<td>1</td>
<td>1.2 (0.8-2.1)</td>
<td>1</td>
<td>1.0 (0.9-1.3)</td>
<td>1</td>
</tr>
<tr>
<td>PE</td>
<td>1.2 (0.9-1.6)</td>
<td>2</td>
<td>4.0 (2.3-7.0)</td>
<td>1</td>
<td>no data</td>
<td>0</td>
<td>1.8 (0.7-4.3)</td>
<td>2</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Abruptio</td>
<td>1.8 (1.1-2.9)</td>
<td>3</td>
<td>6.4 (3.4-12.2)</td>
<td>2</td>
<td>no data</td>
<td>0</td>
<td>1.9 (1.0-3.5)</td>
<td>1</td>
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<td>0</td>
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<tr>
<td>Previa</td>
<td>1.5 (0.8-2.9)</td>
<td>3</td>
<td>no data</td>
<td>0</td>
<td>no data</td>
<td>0</td>
<td>1.1 (0.5-2.4)</td>
<td>1</td>
<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>PPROM</td>
<td>1.3 (1.0-1.7)</td>
<td>3</td>
<td>2.7 (0.1-3.2)</td>
<td>1</td>
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<td>no data</td>
<td>0</td>
</tr>
<tr>
<td>Preterm &lt;37 weeks</td>
<td>1.6 (1.4-1.8)</td>
<td>8</td>
<td>2.4 (1.7-3.3)</td>
<td>4</td>
<td>1.0 (0.7-1.5)</td>
<td>1</td>
<td>1.4 (1.1-1.7)</td>
<td>4</td>
<td>1.1 (1.0-1.4)</td>
<td>4</td>
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<tr>
<td>Preterm &lt;34 weeks</td>
<td>2.5 (1.6-3.9)</td>
<td>4</td>
<td>no data</td>
<td>0</td>
<td>2.0 (1.1-4.0)</td>
<td>1</td>
<td>2.3 (1.5-3.6)</td>
<td>5</td>
<td>no data</td>
<td>0</td>
</tr>
</tbody>
</table>

## Perinatal outcome

<table>
<thead>
<tr>
<th>Event</th>
<th>No data</th>
<th>N</th>
<th>No data</th>
<th>N</th>
<th>2.8 (1.9-4.3)</th>
<th>1</th>
<th>No data</th>
<th>C</th>
<th>No data</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUGR</td>
<td>1.4 (1.0-1.9)</td>
<td>2</td>
<td>2.1 (1.4-3.3)</td>
<td>3</td>
<td>1.1 (1.0-1.2)</td>
<td>1</td>
<td>1.7 (1.0-2.9)</td>
<td>5</td>
<td>1.3 (1.0-1.7)</td>
<td>4</td>
</tr>
<tr>
<td>SGA</td>
<td>1.6 (1.1-2.2)</td>
<td>5</td>
<td>No data</td>
<td>0</td>
<td>1.0 (1.2-2.3)</td>
<td>1</td>
<td>1.7 (1.3-2.2)</td>
<td>3</td>
<td>1.5 (1.3-1.7)</td>
<td>2</td>
</tr>
<tr>
<td>LDW &lt;2500g</td>
<td>2.7 (1.4-5.2)</td>
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<td>No data</td>
<td>0</td>
<td>No data</td>
<td>0</td>
<td>2.0 (1.3-3.2)</td>
<td>3</td>
<td>1.4 (1.0-2.0)</td>
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</tr>
<tr>
<td>LBW &lt;1500g</td>
<td>1.5 (1.1-2.0)</td>
<td>2</td>
<td>1.6 (0.5-5.1)</td>
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<td>No data</td>
<td>0</td>
<td>1.0 (0.8-1.3)</td>
<td>1</td>
<td>1.1 (0.6-2.0)</td>
<td>3</td>
</tr>
<tr>
<td>Cong. malformation</td>
<td>1.1 (1.0-1.3)</td>
<td>1</td>
<td>5.7 (2.5-12.7)</td>
<td>1</td>
<td>No data</td>
<td>0</td>
<td>No data</td>
<td>C</td>
<td>1.2 (0.8-1.7)</td>
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<tr>
<td>5-Mn Apgar score &lt; 7</td>
<td>1.1 (0.8-1.4)</td>
<td>4</td>
<td>2.8 (0.9-8.4)</td>
<td>2</td>
<td>No data</td>
<td>0</td>
<td>No data</td>
<td>C</td>
<td>1.6 (1.0-2.5)</td>
<td>2</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>2.1 (1.0-4.4)</td>
<td>4</td>
<td>2.1 (0.8-4.4)</td>
<td>2</td>
<td>0.9 (0.2-3.3)</td>
<td>1</td>
<td>3.3 (1.3-8.4)</td>
<td>1</td>
<td>1.2 (0.8-1.7)</td>
<td>4</td>
</tr>
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</table>

Data are reported as Odds Ratio (OR) with 95% Confidence Interval (CI); n.d data, no available study.