Intrahepatic Cholestasis of Pregnancy: Relationships Between Bile Acid Levels and Fetal Complication Rates
Glantz et al, Hepatology 2004

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Intrahepatic cholestasis of pregnancy (ICP)

- Pruritus & elevated serum bile acids in 2nd half of pregnancy, resolves after delivery
- Family clustering
- High incidence in Chile, Bolivia, Sweden
- Associated with an increased risk to the fetus
- Aim of this study:
  1. Determine incidence of pruritus/ICP in pregnancy
  2. Determine fetal complication rate according to bile acid levels
Patients and Methods

- Prospective cohort study
- Pregnant women in Västra Götaland, Sweden, 1999-2002
- Inclusion criterion: pruritus without dermatological explanation
- Medical history
  - Heredity for pruritus in pregnancy
  - Outcome of prior pregnancies
  - Skin disorders
  - Atopic & allergic conditions
  - Liver/gallbladder disorders
Study design

- **Weekly visits:**
  1. Pruritus scale (1-10)
  2. Fasting blood sample: total bile acid
      → normal (<10 µmol/L) → check-up in local clinic
      → elevated (> 10 µmol/L = ICP) → department of obstetrics

* weekly: total bile acid, aminotransferases, bilirubin
* weekly: pruritus scale
* weekly: fetal monitoring with cardiotocography (ctg)
→ no other specific instructions

- Data at delivery collected
45,485 deliveries

937 women with pruritus in pregnancy included

820 women completed study until parturition

690 women observational study

117 women lost to follow-up

130 women intervention study

No ICP bile acids <10 µmol/L n=185

Mild ICP bile acids 10–39 µmol/L n=409

Severe ICP bile acids ≥40 µmol/L n=96

No ICP n=58

Mild ICP n=59
Incidence of Pruritus of 2.1%
Incidence of pruritus of 2.1%

Incidence of ICP of 1.5%
- 81% mild ICP
- 19% severe ICP
Results: previous pregnancies

**White bar** indicates no ICP (serum bile acids <10 mol/L)

**Gray bar** indicates mild ICP (bile acids 10-39 mol/L)

**Black bar** indicates severe ICP (bile acids ≥ 40 mol/L).
Results: previous pregnancies

25% of severe ICP group had a preterm delivery (vs 4% in non ICP group)

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Results: previous pregnancies

25% of severe ICP group had a preterm delivery (vs 4% in non ICP group)

4.1 % of severe ICP group had IUFD (vs 0.6% in non ICP group)

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Black bar indicates severe ICP (bile acids ≥ 40 mol/L).
Results: gallstone disease/heredity for pruritus of pregnancy

- **Gallstone disease**
  - 24 women, 2.9%
  - No ICP group: 0.5% prevalence
  - Mild ICP group: 2.3% prevalence
  - **Severe ICP group**: 7.4% prevalence

- **Heredity for pruritus of pregnancy**
  - 173 women, 21%
  - No ICP group: 13%
  - Mild ICP group: 21%
  - **Severe ICP group**: 30%
Results: Fetal complications

- Spontaneous preterm delivery in 4.3%
- Meconium staining of amniotic fluid in 24.8%
- Green staining of placenta/membranes in 12.2%
- Asphyxial events in 7.1%

White bar: no ICP. Gray bar: mild ICP. Black bar: severe ICP.
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High complication rate in severe ICP group/bile acid level > 40 µmol/L

White bar: no ICP. Gray bar: mild ICP. Black bar: severe ICP.
Fig. 3. Probability of (A) preterm deliveries, (B) asphyxial events, (C) meconium staining of amniotic fluid, and (D) green staining of placenta and membranes in relation to serum bile acid levels (μmol/L) analyzed with simple logistic regression (thick line) and spline functions (medium line), the latter with 95% CI (thin line).
Critical bile acid level: 40 µmol/L!

Fig. 3. Probability of (A) preterm deliveries, (B) asphyxial events, (C) meconium staining of amniotic fluid, and (D) green staining of placenta and membranes in relation to serum bile acid levels (µmol/L) analyzed with simple logistic regression (thick line) and spline functions (medium line), the latter with 95% CI (thin line).
Conclusion

• Pruritus in 2.1 %, ICP in 1.5 %
• Probability of fetal complications increases 1-2% for each µmol/L of bile acid
• But: complications occur not until bile acid ≥ 40 µmol/L
• In 81% mild ICP without increased fetal complications
• In 19% severe ICP with increased fetal risk
• → Surveillance with bile acid level
  ▫ Manage expectantly when levels < 40 µmol/l
  ▫ Manage actively (induction of labor) when levels ≥ 40 µmol/l
Discussion

- Prove of relationship between the severity of ICP and fetal complications
- Bile acid level distinguishing 2 degrees of risk
- IUFD not elevated (increased attention?)
- Correlation between gallstone disease & ICP
DON'T IGNORE THE ITCH

Intense itching is not normal.

It could be ICP and it could put your baby's life at risk.
Spline function

Beispiel eines Splines mit 8 Knoten