Pregnancy and hemodialysis

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Introduction

• Delay pregnancy until transplantation?
  – Reduced fertility
  – High rate of complications

• But long wait times in transplantation:
  – Organ shortage
  – Immunisation

• Increased successful pregnancy: intensive hemodialysis
Fertility

• **Decrease in fertility** due to:
  – Decrease of libido
  – Anovulation
  – Dysregulation of the menstrual cycle

• LH increased
  – but LH surge necessary for ovulation absent

• High serum **prolactin** levels
  – Due to decreased kidney prolactin clearance

• Estrogens and progesterone levels decreased
  – Secondary abnormalities in endometrial morphology
Evolution

- First case of pregnancy on dialysis in 1971
- In the 1990’s, only 42% of young women reported menstruating
- Daily dialysis could improve fertility
Results of pregnancies

• In 1980, EDTA reported that only 23% of 115 pregnancies in dialysis ended with a baby alive

• Bagon et al, AJKD, 1998
  – Success 50%
  – Correlation between birth weight and dose of dialysis
<table>
<thead>
<tr>
<th>Author</th>
<th>Period</th>
<th>N</th>
<th>% live birth</th>
<th>Gestation</th>
<th>Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chao</td>
<td>1990-2000</td>
<td>18</td>
<td>69</td>
<td>32 (23-36)</td>
<td>1542 (512-2660)</td>
</tr>
<tr>
<td>Eroglu</td>
<td>2000-2002</td>
<td>7</td>
<td>86</td>
<td>32 (26-36)</td>
<td>1400 (420-2640)</td>
</tr>
<tr>
<td>Haase</td>
<td>2000-2004</td>
<td>5</td>
<td>100</td>
<td>32.8±3.3</td>
<td>1765±554</td>
</tr>
<tr>
<td>Barua</td>
<td>2001-2006</td>
<td>7</td>
<td>100</td>
<td>36±3</td>
<td>2417±657</td>
</tr>
<tr>
<td>Luders</td>
<td>1988-2008</td>
<td>52</td>
<td>87</td>
<td>32.7±3.1</td>
<td>1554±663</td>
</tr>
<tr>
<td>Bahadi</td>
<td>1999-2008</td>
<td>9</td>
<td>56</td>
<td>35 (34-36)</td>
<td>2380 (1800-2900)</td>
</tr>
<tr>
<td>Asamiya</td>
<td>1986-2007</td>
<td>33</td>
<td>64</td>
<td>28.3±9</td>
<td>1414±759</td>
</tr>
<tr>
<td>Chou</td>
<td>1990-2006</td>
<td>13</td>
<td>50</td>
<td>30.8±1.6</td>
<td>1511±284</td>
</tr>
<tr>
<td>Tan</td>
<td>1995-2004</td>
<td>11</td>
<td>82</td>
<td>31 (26-36)</td>
<td>1390±705</td>
</tr>
<tr>
<td>Lucianini</td>
<td>1988-1998</td>
<td>5</td>
<td>80</td>
<td>28.6±4</td>
<td>1431±738</td>
</tr>
<tr>
<td>Hladunewich</td>
<td>2000-2013</td>
<td>22</td>
<td>86.4</td>
<td>36 (32–37)</td>
<td>2118±857</td>
</tr>
<tr>
<td>Shahir</td>
<td>1966-2008</td>
<td>49</td>
<td>79</td>
<td>46.6% &gt;37</td>
<td>2131 (800–4200)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26.7% &lt; 32</td>
<td></td>
</tr>
<tr>
<td>Moranne</td>
<td>1995-2001</td>
<td>7</td>
<td>83</td>
<td>31 (24-34)</td>
<td>1495 (660-1920)</td>
</tr>
</tbody>
</table>
Brazilian single-center report

- 52 pregnancies between 1988 and 2008
- >50% conception before dialysis initiation
- Dialysis time: 12 to 18h/week
- Significant urine output: mean 1000 ml
- 86.5% live birth rate
- Mean gestational age 32.7±3.1 weeks
- Mean weight: 1554±663g
- Pre-eclampsia: 19%
- Polyhydramnios: 40%
- HTA: 70%

Luders et al, AJKD, 2010
### Table 4. Univariate Logistic Regression Models for Risk of an Adverse Fetal Outcome

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
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<tr>
<td>Pre-eclampsia</td>
<td>24.0 (4.1-141)</td>
<td>&lt;0.001</td>
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<tr>
<td>Third-trimester Hct (1-IU increase)</td>
<td>0.86 (0.74-0.99)</td>
<td>0.04</td>
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<td>Polyhydramnios</td>
<td>0.17 (0.03-0.84)</td>
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<td>Predialysis serum urea (1-IU increase)</td>
<td>1.03 (1.00-1.05)</td>
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<td>Predialysis serum urea &lt;75 mg/dL</td>
<td>0.21 (0.04-1.05)</td>
<td>0.06</td>
</tr>
<tr>
<td>stdKt/V</td>
<td>0.86 (0.28-2.59)</td>
<td>0.8</td>
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Luders et al, AJKD, 2010
Australia 1966–2008

49 pregnancies
79% live birth
53% preterm
19% preeclampsia

65%<2,5kg
35%<1,5kg

Sahir et al, Nephrology, 2013
Meta-analysis

• 90 pregnancies in 78 patients
• Healthy offspring: 76% (50 à 100%)
• Fœtal risk:
  - Intrauterine death
    5 spontaneous abortions, 14 still-births or neonatal deaths
    /80 pregnancies
  - Hydramnios: 18 à 100%
  - Small-for-gestational-age: ±100%
  - Preterm: 67 à 100%
• Daily dialysis at least 24 h/wk

Piccoli et al, CJASN, 2010
Intensive dialysis

- Average dialysis time >24 hours/week
- Live birth rates of 100%
- 5 women treated with in-center HDF
- Mean dialysis time of 28.6 h/week
  - 6 sessions of 4 to 5 hours
  - 1 conceived before dialysis initiation/others already on chronic dialysis
  - 2 had significant urine output

Haase et al, NDT, 2005
Intensive dialysis

All delivered live infants
Mean gestational age **32 weeks**
Mean weight of **1765 ± 554 g**
Predialysis urea levels were <49 mg/dL

Haase et al, NDT, 2005
Nocturnal dialysis

- Nocturnal HD center in Toronto
- 7 pregnancies among 5 women (2001 and 2006)
- Weekly dialysis time of $36 \pm 10$ hours preconception
  - increased to $48 \pm 5$ hours during pregnancy for a typical schedule of 5 to 7 nights per week

Barua et al, CJASN, 2008
Nocturnal dialysis

- Mean gestational age $36.2 \pm 3$ weeks
  - only 1 infant delivered <36 weeks
- Birth weight:
  - from 1260 g for the 30-week infant
  - to 3000 g for an infant delivered at term
  - Mean birth weight of $2417.5 \pm 657$ g
Nocturnal dialysis

- High clearance of urea and other uremic toxins
- Partly restore the normal function of the pituitary hypothalamic axis
- Better control of blood pressure

Barua et al, CJASN, 2008
Intensive Hemodialysis Associates with Improved Pregnancy Outcomes: A Canadian and United States Cohort Comparison

Intensive dialysis

Live birth rates by dialysis intensity

Live Birth Rate %

Tertile 1 (0 - 20) 48%
Tertile 2 (21 - 36) 75%
Tertile 3 (37 - 56) 85%

N-Size: 46 16 13

Hladunewich M A et al. JASN, 2014
Intensive dialysis

Time-to-event analysis by dialysis intensity

Hladunewich M A et al. JASN, 2014
Intensive dialysis

Gestational age and birth weight by dialysis intensity

A

Gestational Age (weeks)

Tertile 1
(0 - 20)

Tertile 2
(21 - 36)

Tertile 3
(37 - 56)

Hours of Hemodialysis

B

Birth Weight (grams)

Tertile 1
(0 - 20)

Tertile 2
(21 - 36)

Tertile 3
(37 - 56)

Hours of Hemodialysis

Hladunewich M A et al. JASN, 2014
Importance of low urea level

- 33 pregnancies
- 64% successful pregnancies

Asamiya et al, KI, 2009
Urea and prognosis

Association between birth weight, gestational age and maternal blood urea nitrogen (BUN) level

- A birth weight of 1500 g corresponded to a BUN level of 49.0 mg/100 ml=8.2 mmol/l
- A gestational age of 32 weeks corresponded to a maternal BUN level of 48.0 mg/100 ml=8.0 mmol/l

Asamiya et al, KI, 2009
Polyhydramnios

- Polyhydramnios: 18% to 100%
  - result of fetal solute diuresis secondary to a high urea concentration
  - reversal of polyhydramnios with an increase in dialysis time
  - no cases of polyhydramnios in intensive program
**Hemoglobin**

- Impact of anemia on pregnancy prognosis in general population

- The average of Hb level is significantly higher in the successful group than in the unsuccessful group
  - $9.6 \pm 0.9$ versus $8.3 \pm 1.9$ g/100 ml, $P=0.036$

Asamiya et al, KI, 2009
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Luders et al, AJKD, 2010
Anemia

- Increased **EPO** requirements
  - Doubling of the baseline EPO requirements frequent

- Increased **iron** requirements
  - expected in healthy pregnant women
  - more pronounced in pregnant women on dialysis

- Placental growth, blood loss from intensive dialysis, and inflammation due to cytokines:
  - EPO resistance
  - increased iron requirements
Anemia

• Aggressive EPO and iron therapy should allow avoidance of blood transfusions
• Oral and intravenous iron as well as EPO are safe in pregnancy
• Complete blood count and iron stores levels should be closely monitored
Outcomes according to dialysis commencing before or after conception

- 77 pregnancies / 73 women
  - 53 conceived after long-term dialysis
  - 24 occurred before dialysis began
- 73% live birth rate
- Median gestational age 33.8 weeks (30.6–37.6)
- Median birthweight 1750 g (1130–2417 g)

Jesudason et al, CJASN, 2014
Gestational age and birth weight according to timing of conception before dialysis (CBD) or conception on dialysis (COD)

Women who conceived before dialysis had significantly higher live birth rates: 91% versus 63%; $P=0.03$

This difference was primarily due to higher rates of early pregnancy loss before 20 weeks in women who conceived after dialysis was established

Jesudason et al. CJASN 2014
Maternal complications : HTA

• 20 to 70%
  – Varied definitions

• Lower prevalence in the intensive cohorts
  – Augmented control of volume status
  – May have an impact on pregnancy outcome
Maternal complications: HTA

<table>
<thead>
<tr>
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<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Systolic blood</td>
<td>122 ± 24</td>
</tr>
<tr>
<td>pressure (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood</td>
<td>75 ± 20</td>
</tr>
<tr>
<td>pressure (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Postdialysis weight</td>
<td>56.5 ± 4</td>
</tr>
<tr>
<td>(kg)</td>
<td></td>
</tr>
</tbody>
</table>

Barua et al, CJASN, 2008
More common in dialysis patients

Preeclampsia =
  - hypertension after 20 weeks of gestation with proteinuria
  - typical associated symptoms (epigastric pain, visual changes, severe headache, eclampsia)
  - abnormal uterine artery Doppler waveforms
Diagnosis of preeclampsia

- Cannot rely on the finding of proteinuria
- Any unexplained rise in blood pressure after 20 weeks of pregnancy
- Classic preeclampsia symptoms
- Laboratory abnormalities consistent with HELLP syndrome
Table 3. Descriptive Data for Fetal Outcome According to the Presence of Pre-eclampsia

<table>
<thead>
<tr>
<th></th>
<th>Absent (n = 42)</th>
<th>Present (n = 10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful pregnancies</td>
<td>39 (92.9)</td>
<td>6 (60)</td>
<td>0.02</td>
</tr>
<tr>
<td>Preterm delivery*</td>
<td>32 (82.0)</td>
<td>9 (100)</td>
<td>0.7</td>
</tr>
<tr>
<td>Preterm delivery &lt; 30 wk*</td>
<td>3 (7.7)</td>
<td>7 (77.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>28 (66.7)</td>
<td>6 (60.0)</td>
<td>0.5</td>
</tr>
<tr>
<td>No. of SGA</td>
<td>18 (43)</td>
<td>6 (60)</td>
<td>0.5</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>33.6 ± 3.1</td>
<td>28.9 ± 2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1,721 ± 601</td>
<td>852 ± 412</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*P values calculated using Fisher’s exact test.
Management of a pregnancy in HD

- Close collaboration among the nephrologist, obstetrician, nutritionist…
- **Diagnosis of pregnancy** complex and can be delayed (irregular menstrual cycles)
- False-positive pregnancy tests can occur:
  - hCG cleared by the kidneys and can accumulate
- Caution when evaluating the first trimester Down syndrome screening test
Management of a pregnancy in HD

- **Medication review** to discontinue teratogenic drugs
  - renin-angiotensin system blockers
- **Nutritionists** should be involved to assess the patient’s nutritional status and follow her throughout her pregnancy
- **Diet and caloric intake** need not be limited during pregnancy
  - especially when accompanied by intensive HD
Management of a pregnancy in HD

- **Protein intake** should be increased to a minimum of 1.1 g/kg/day
  - standard recommendation for a pregnant woman
  - taking into account a possible superimposed loss of amino acids in the dialysate with intensive dialysis

- **Folic acid**
  - as for every pregnant woman
  - at a higher dose of 5 mg daily

- **Minerals and water-soluble** vitamins should also be given at increased doses
  - can be partially removed by intensive dialysis
Management of a pregnancy in HD

- **Dialysate calcium** concentration: to be increased to 1.75 mmol/L,
  - predialysis and postdialysis calcium level closely followed
  - to avoid hyper- and hypocalcemia
  - to ensure adequate stores for fetal skeletal development

- **Serum parathyroid hormone and phosphate levels** need to be monitored
  - with additional phosphate added as necessary
  - hypophosphatemia can occur because
    - intensive dialysis
    - increased phosphate requirements for fetal bone formation
Management of a pregnancy in HD

- **Dialysate bicarbonate** levels may be reduced
  - to ensure the physiologic expression of respiratory alkalosis associated with pregnancy
- **Potassium** concentration in dialysate must be adjusted
  - to reflect the more intensive HD regimen
  - usually with a concentration of 3.0 mEq/L
Management of a pregnancy in HD

• Assessment of **target weight**: can be a challenge
  – Weight gain usually minimal during the first trimester
  – Increases up to 0.5 kg/week during the second and third trimesters
  – Weekly reassessment of target weight to prevent fluid overload as well as intradialytic or postdialysis hypotension

• Blood pressure should be kept as stable as possible and lower than 140/90 mmHg
Ultrasonographic assessments

- **Feto- and uteroplacental circulation**
  - Increased resistance in the Doppler flow assessment in the uterine arteries between 17 and 22 weeks may identify poor placentation and pregnancies at greater risk of preeclampsia and fetal growth restriction.

- **Cervical length measurements**
  - Used to predict risks preterm labor.

- **Detection of oligohydramnios or polyhydramnios**
  - Direct relationship between maternal intravascular volume and amniotic fluid volume.

- **Serial ultrasounds are initiated in the third trimester**
  - On a weekly schedule.
  - Fetal well-being and adequate fetal growth.
Conclusion

• Pregnancy in a dialysis patient is a serious event with deep implications for the patient, her child, and the medical team
• Recent data with intensive HD are promising with a higher conception rate, more favorable outcomes for mother and infants