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’, 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

Author	Period	N	% live birth	Gestation	Weight (g)
Chao	1990-2000	18	69	32 (23-36)	1542 (512-2660)
Eroglu	2000-2002	7	86	32 (26-36)	1400 (420-2640)
Haase	2000-2004	5	100	32,8±3,3	1765±554
Barua	2001-2006	7	100	36±3	2417±657
Luders	1988-2008	52	87	32,7±3,1	1554±663
Bahadi	1999-2008	9	56	35 (34-36)	2380 (1800-2900)
Asamiya	1986-2007	33	64	28,3±9	1414±759
Chou	1990-2006	13	50	30,8±1,6	1511±284
Tan	1995-2004	11	82	31 (26-36)	1390±705
Malik	1992-2003	12	58	31,5 (27-36)	1700 (1115-2300)
Luciani	1988-1998	5	80	28,6±4	1431±738
Hladunewich	2000-2013	22	86,4	36 (32–37)	2118±857
Shahir	1966-2008	49	79	46,6% >37 26,7% < 32	2131 (800–4200)
Moranne	1995-2001	7	83	31 (24-34)	1495 (660-1920)

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

Brazilian single-center report

Table 4. Univariate Logistic Regression Models for Risk of an Adverse Fetal Outcome

	OR (95% CI)	*P*
Pre-eclampsia	24.0 (4.1-141)	<0.001
Third-trimester Hct (/1-IU increase)	0.86 (0.74-0.99)	0.04
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Predialysis serum urea <75 mg/dL	0.21 (0.04-1.05)	0.06
stdKt/V	0.86 (0.28-2.59)	0.8

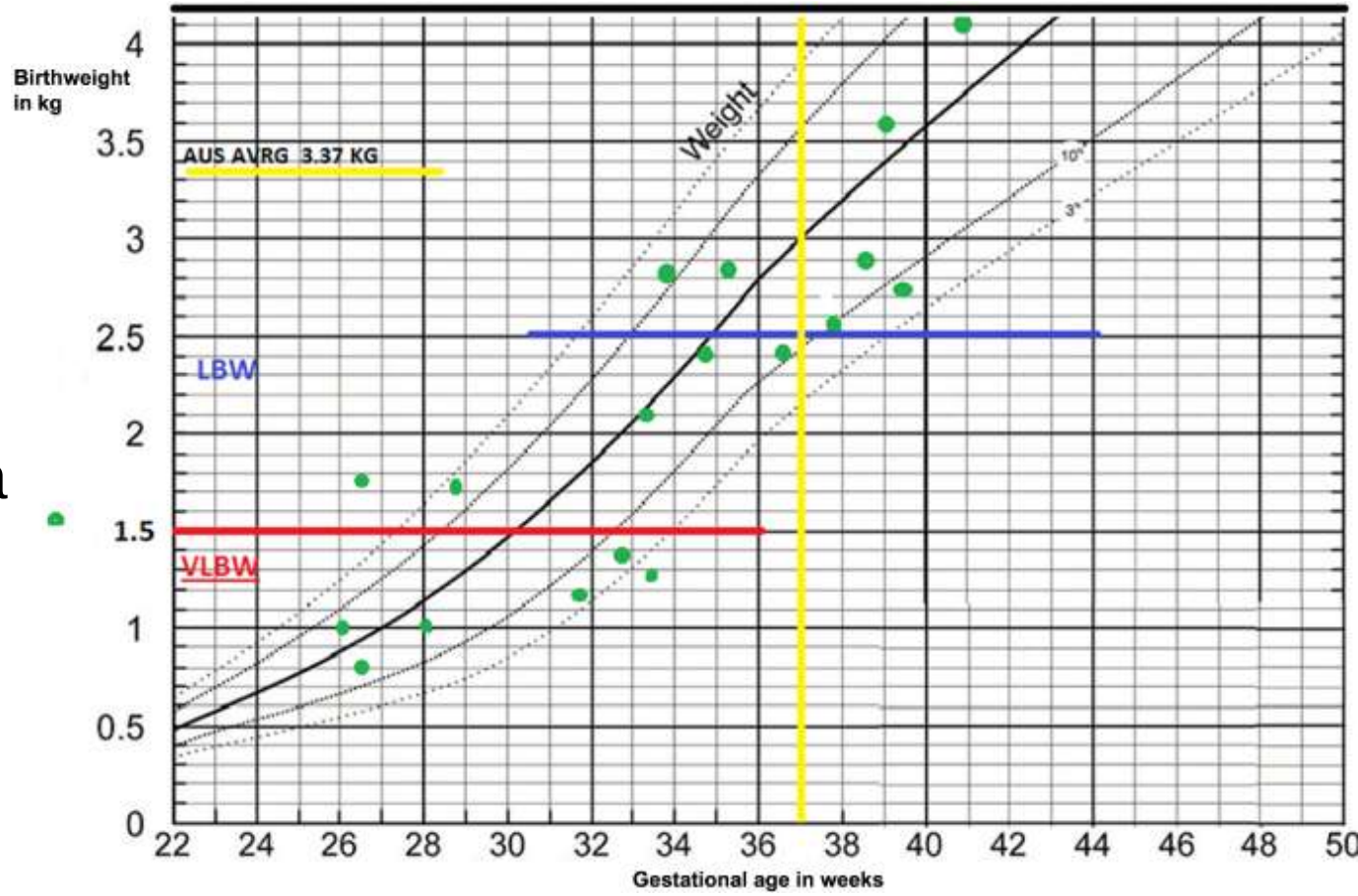
Luders et al, AJKD, 2010

ANZDATA registry

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

Patient	Birth at gestational age (weeks)	Weight/length (g/cm)	APGAR/ umbilical pH	Complications/management	LOS on ICU/in hospital (days)	Outcome
1	30+4	1274/37	7/8/9/7.28	Respiratory dysfunction/3 days CPAP+theophylline	13/27	5 years, healthy
2	31+5	2215/46	2/7/8/7.21	Respiratory dysfunction/2 days CPAP+theophylline. Hyperbilirubinaemia/phototherapy	3/8	4 years, healthy
3	30+0	1240/38	4/7/9/7.14	IRDS+respiratory acidosis/5 days ventilation+CPAP+surfactant+ theophylline. Pneumothorax/chest tube. Hyperbilirubinaemia/phototherapy	13/35	2 years, healthy
4	37+4	2465/48	9/10/10/7.22	Hypoglycaemia/dextrose solution	4/9	10 months, healthy
5	34+4	1630/42	8/9/9/7.33	Respiratory dysfunction/1 day CPAP+ theophylline. Systemic infection/i.v. antibiotics. Hyperbilirubinaemia/ phototherapy	50/52	8 months, healthy

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 ±10 hours preconception
  - increased to 48 ± 5 hours during pregnancy for a typical schedule of 5 to 7 nights per week

Barua et al, CJASN, 2008

Nocturnal dialysis

Table 1. Pregnancy outcomes[a]

	Number of Weeks at Delivery	Mode of Delivery	Baby's Birth Weight (g)	Baby's APGAR Scores at 1 and 5 min
Patient 1	36	C/S	2020	9/9
Patient 2: Pregnancy 1	38	SVD	3000	5/8
Patient 2: Pregnancy 2	37^{4}	SVD	2785	9/9
Patient 3	36^{5}	Induced labor, vacuum extraction	2690	6/9
Patient 4	38^{5}	C/S	2750	8/9
Patient 5	30	SVD	1260	5/7

[a]C/S, cesarean section; SVD, spontaneous vaginal delivery. Superscript numerals indicate days.

- Mean gestational age 36.2 ± 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 ± 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

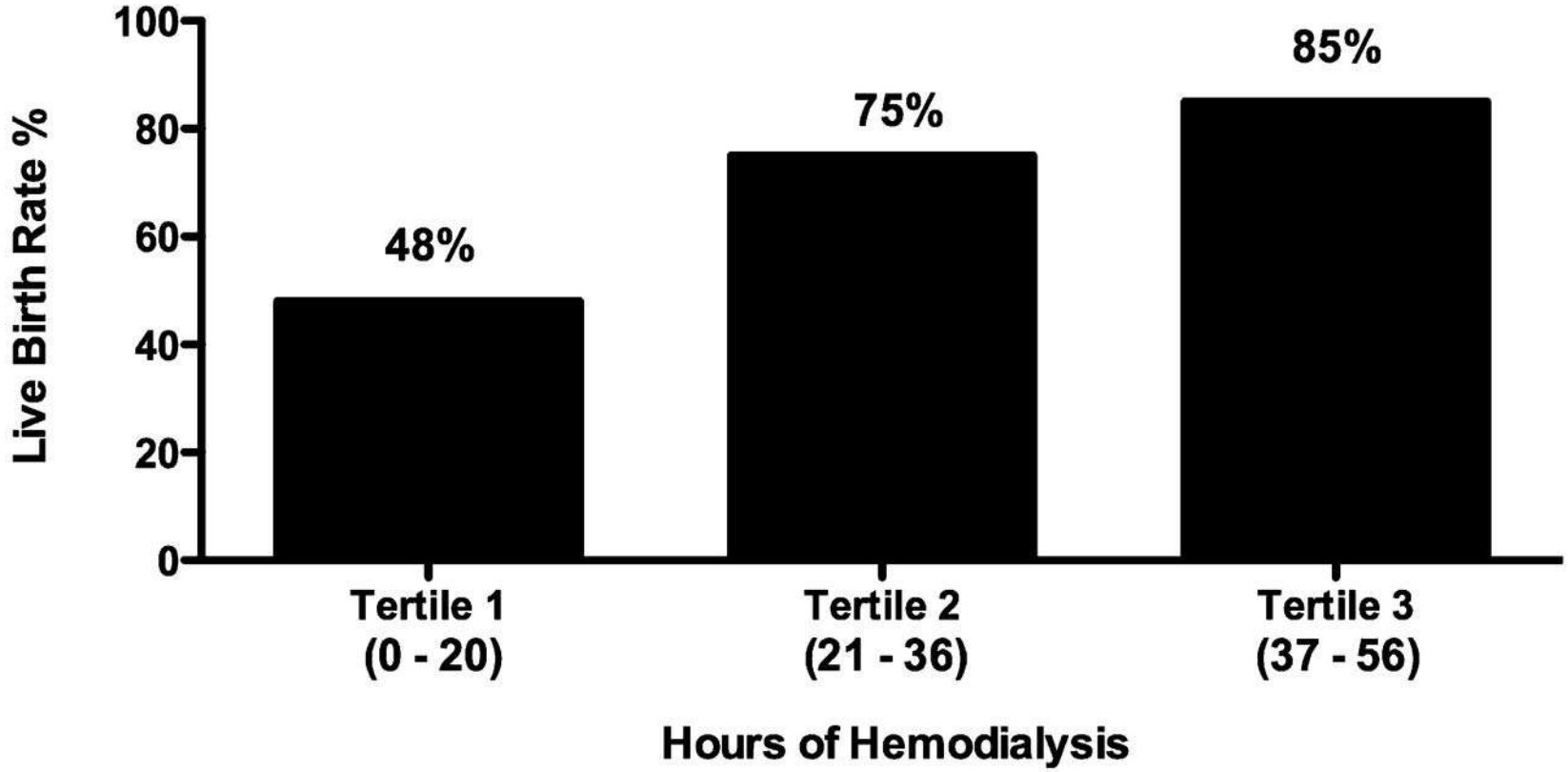
Barua et al, CJASN, 2008

Intensive Hemodialysis Associates with Improved Pregnancy Outcomes: A Canadian and United States Cohort Comparison

Comparison of pregnancy outcomes from 22 pregnancies in Toronto (2000–2013) with outcomes from 70 pregnancies in the American Registry for Pregnancy in Dialysis Patients (1990–2011)

Intensive dialysis

Live birth rates by dialysis intensity

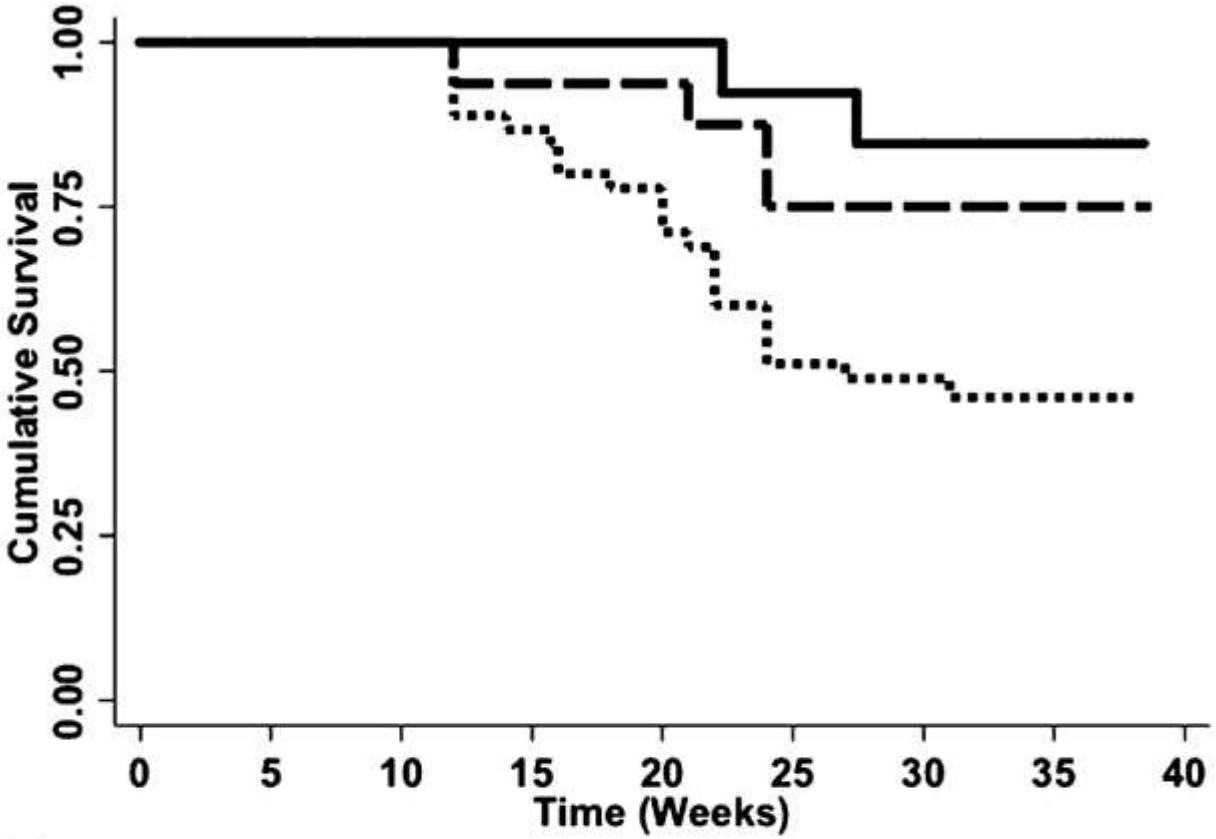


N-Size:	46	16	13

Hladunewich M A et al. JASN, 2014

Intensive dialysis

Time-to-event analysis by dialysis intensity

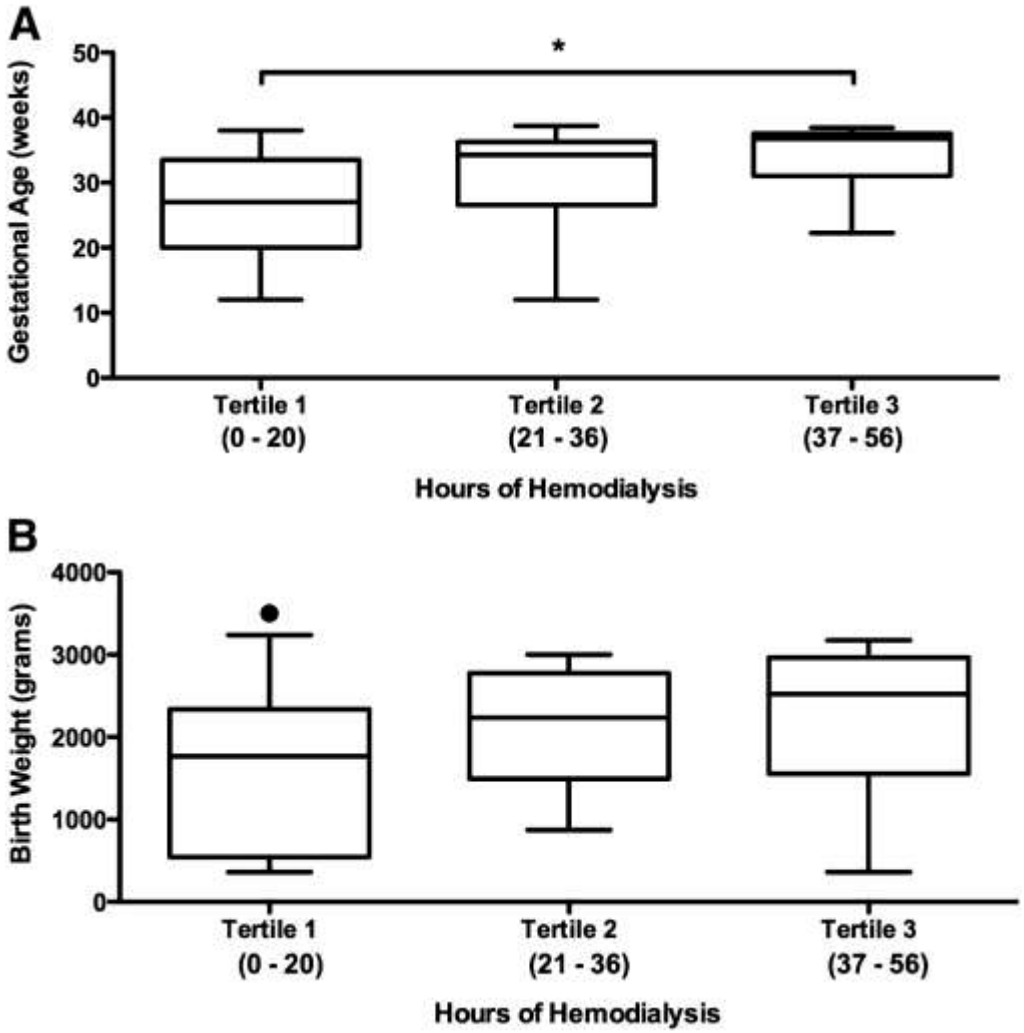


Number at risk					
0-20 Hours (·····)	45	45	35	17	0
21-36 Hours (— —)	16	16	15	11	0
37-56 Hours (——)	13	13	13	11	0

Hladunewich M A et al. JASN, 2014

Intensive dialysis

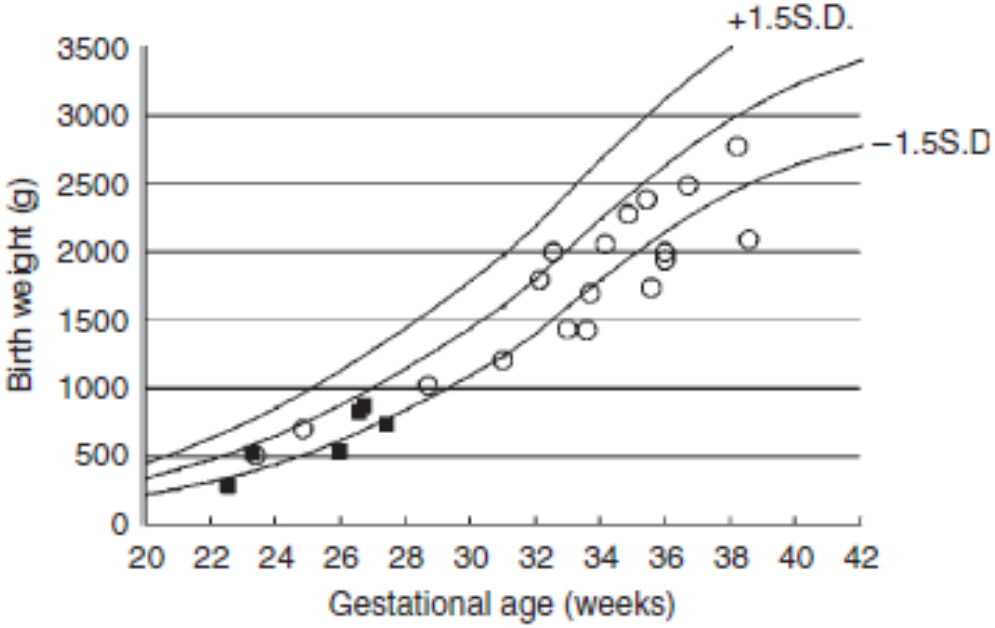
Gestational age and birth weight by dialysis intensity



Hladunewich M A et al. JASN, 2014

Importance of low urea level

- 33 pregnancies
- 64% successful pregnancies



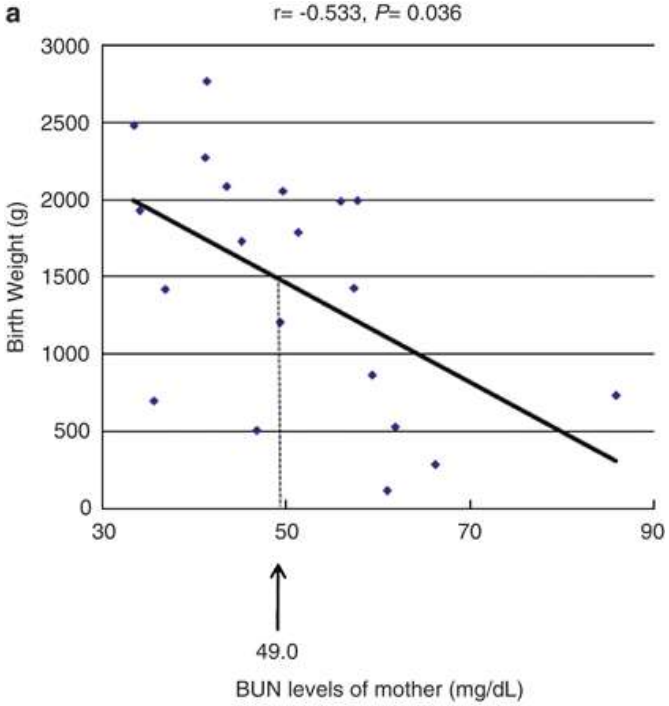
Asamiya et al, KI, 2009

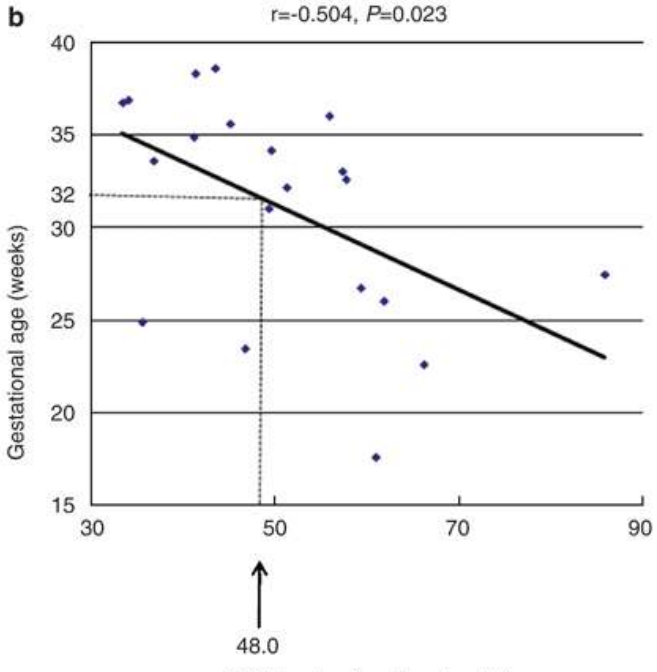
Urea and prognosis

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 mmoll
- 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±0.9 versus 8.3±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

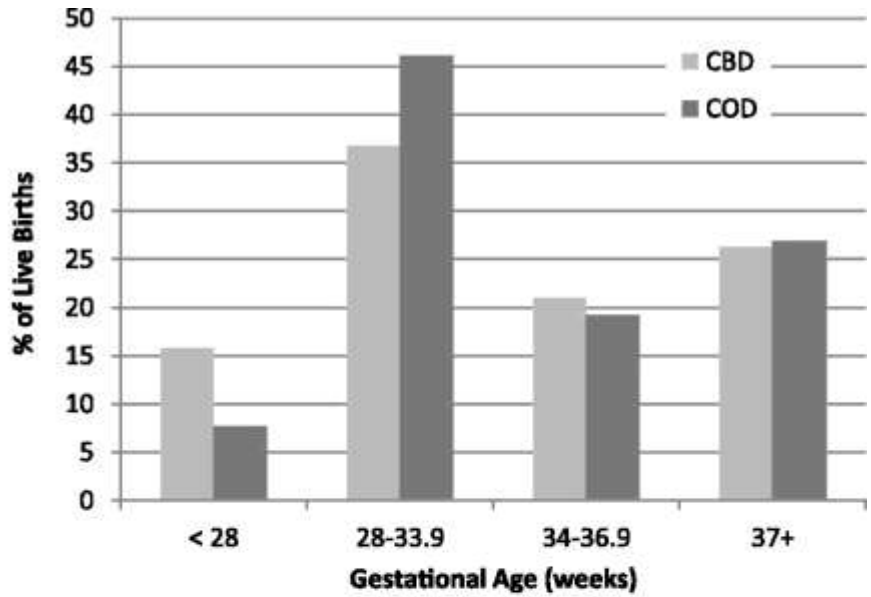
- Aggressive EPO and iron therapy should allow avoidance of blood transfusions
- Oral and intravenous iron as well as EPO are safe in pregnancy
- Complete blood count and iron stores levels should be closely monitored

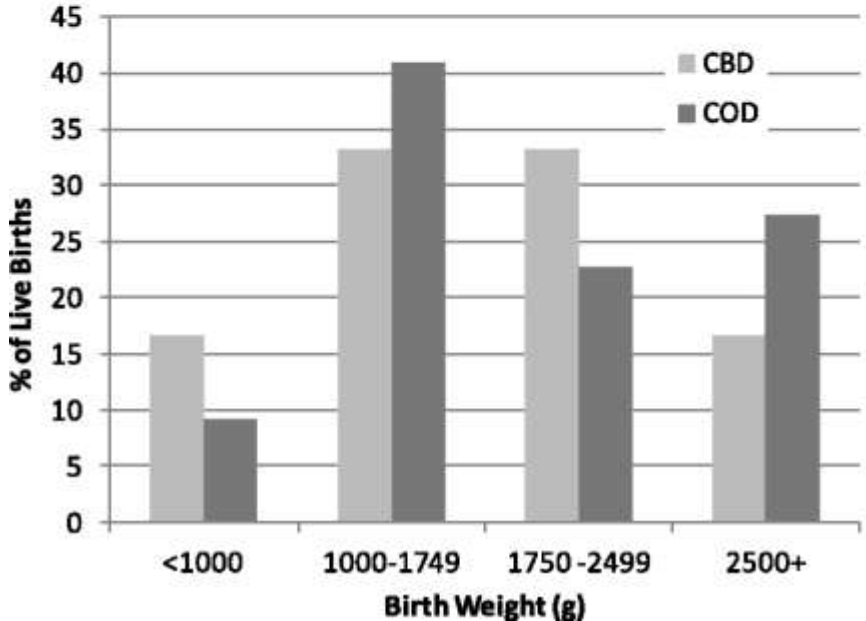
Outcomes according to dialysis commencing before or after conception

- 77 pregancies /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

	Month								
	1	2	3	4	5	6	7	8	9
Systolic blood pressure (mmHg)	122 ± 24	119 ± 15	114 ± 10	118 ± 10	119 ± 11	112 ± 18	122 ± 16	117 ± 21	117 ± 24
Diastolic blood pressure (mmHg)	75 ± 20	76 ± 15	74 ± 10	81 ± 12	79 ± 12	73 ± 11	72 ± 9	80 ± 10	77 ± 11
Postdialysis weight (kg)	56.5 ± 4	57.5 ± 5	57.5 ± 5	58.7 ± 4	60.4 ± 5[a]	64.0 ± 6[a]	67.2 ± 7[a]	69.5 ± 7[a]	72.3 ± 9[a]

Barua et al, CJASN, 2008

Preeclampsia and HELLP Sd

- 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

Preeclampsia and HELLP Sd

Table 3. Descriptive Data for Fetal Outcome According to the Presence of Pre-eclampsia

	Pre-eclampsia		
	Absent (n = 42)	**Present (n = 10)**	***P***
Successful pregnancies	39 (92.9)	6 (60)	0.02
Preterm delivery[a]	32 (82.0)	9 (100)	0.7
Preterm delivery <30 wk[a]	3 (7.7)	7 (77.8)	<0.001
Cesarean delivery	28 (66.7)	6 (60.0)	0.5
No. of SGA	18 (43)	6 (60)	0.5
Gestational age (wk)	33.6 ± 3.1	28.9 ± 2.6	<0.001
Birth weight (g)	1,721 ± 601	852 ± 412	<0.001

Luders et coll, AJKD, 2010

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