



### PREGNANCY AND DIALYSIS

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- Infertility among CKD patients
- Pregnancy of Dx patients
- Dx prescription
- Labor
- Fetal outcome



## **CKD AND PREGNANCY**

- CKD stage 1-2
- eGFR <u>>60 mL/min/1.73 m<sup>2</sup></u>
- Successful pregnancy
- No adverse effect on CKD





# **CKD AND PREGNANCY**

- Historically (before 1975) pregnancy was discouraged for women with CKD and early termination advised
- "children of women with renal disease used to be born dangerously or not at all – not at all if their doctors had their way.....nature takes a helping hand by blunting fertility as renal function falls"



# **CKD AND PREGNANCY**

• 'Show me a method of birth control more

effective than end stage renal disease'

• 'Even if a woman on CAPD ovulates, doesn't

the egg just float away?'



Rodby, 1991 Rodby, 1992

# INFERTILITY

- Dysregular mensturial cycles GFR< 15 ml/min
- Amenorea GFR< 5 ml/min
- Secondary changes of the morphology of the endometrium
  - Atrophy
  - Proliferative changes



#### INFERTILITY

- Elevated prolactin
- Reduced estrogen and LH
- Anovulation
- Early menopause (47 years of age)



Adv Chronic Kidney Dis 2013;20(5):411-8

#### **Frequency of Conception**

Pregnancies 1992-1995
 Hemodialysis
 Peritoneal Dialysis

135 (2.2%) 109 (2.4%) 18 (1.1%)\*

\*p<.01

World Congress of Nephrology, 2003

#### The first cases of pregnant

#### woman on HD ever published were by

#### Herwig et al. in 1965 and Orme et al. in 1968.





Full Term Pregnancy and Successful Delivery in a Patient on Chronic Haemodialysis P CONFORTINI, G GALANTI, G ANCONA, A GIONGO, E BRUSCHI, E LORENZINI Istituti Ospedalieri, Verona, Italy





Proc Eur Dial Transplant Assoc 1971:74-80

#### OPEN DISCUSSION

MIGONE (Chairman): Thank you very much for your very interesting paper. Is this case of pregnancy after several years of regular dialysis treatment the only one in the world? I would like to ask if anyone from the floor has seen anything like it?

A C KENNEDY (Glasgow): I think the Verona group deserve to be complimented for two reasons, first of all for the successful outcome of the preg-

to us all. The second reason I think they deserve compliments is that they are able to put their patients onto regular dialysis when their creatinine clearance is still 8 or 9 ml/min. I think this second point probably is the reason for the successful outcome of the pregnancy in their case; and I wonder if it is the policy in Verona to establish patients on regular dialysis when they still have such (relatively speaking) large degree of their renal function left?



- ✓ Improvement in Dx technologies
- Close follow up of patients
- ✓ Multidisciplinary approach
- In 2000 >15,000 premenapousal female
  HD patients worldwide



- EDTA 1980 report:
- 115 pregnancies
- 23% were viable



Clinical Nephrology, Vol. 59 - No. 5/2003 (379-382)

# The outcome of pregnancy among patients receiving hemodialysis treatment

R. Kazancioglu<sup>1</sup>, S. Sahin<sup>1</sup>, R. Has<sup>2</sup>, A. Turkmen<sup>1</sup>, H. Ergin-Karadayi<sup>3</sup>, L. Ibrahimoglu<sup>2</sup> and S. Bozfakioglu<sup>1</sup>

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#### 3 patients (2 prevelant HD, 1 incident HD)



- Recent publications report pregnancy in 1–7% in women on chronic dialysis
- Pregnancy in contemporary women on dialysis is more likely to be successful, with 30–50% of pregnancies resulting in delivery of a surviving infant





#### State Paul de

#### Pregnancy in Dialysis Patients: Is the Evidence Strong Enough to Lead Us to Change Our Counseling Policy?

Georgina Badura Peccele," Anne Conipe," Valentina Consiglies," Elena Vasarie," Rossella Antes," Maria Chiara Desposite," Salcatore Beatempo," and Tallia Totros" "Designed and Cloud Sciences University of Ser Logic Orlinson, Toron Boly and "Manual and Univ

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Original Articles



Pregnancy in dialysis potients in the new millennium: a systematic review and meta-regression analysis correlating dialysis schedules and pregnancy outcomes.

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17th International Congress of Hephrology, Bolytes, and Tompsonitation



Leading European Nephrology

Clinical Kidney Journal, 2017, vol. 10, no. 2, 276–281

doi: 10.1093/ckj/sfw130 Advance Access Publication Date: 5 January 2017 Original article

#### ORIGINAL ARTICLE

#### Pregnancy outcomes in women on hemodialysis: a national survey

#### Mala Sachdeva, Valerie Barta, Jyotsana Thakkar, Vipulbhai Sakhiya and Ilene Miller

Department of Medicine, Division of Kidney Diseases and Hypertension, North Shore University Hospital and Long Island Jewish Medical Center, Hofstra Northwell School of Medicine, Great Neck, NY, USA

- A total of 196 nephrologists responded to the survey, reporting >187 pregnancies.
- Of the respondents, 45% had cared for pregnant
- females on HD and 78% of pregnancies resulted in live births.
- In 44% of the pregnancies a diagnosis of preeclampsia was made.
- There were no maternal deaths.







Shah et al JASN 2019

#### **DIAGNOSING PREGNANCY**

- Even if there is sufficient residuel renal
  - function the urine tests for pregnancy is inconclusive
- Serum β chorionic gonadothropine level is not conclusive
- Resistance to ESA therapy

Ultrasonographic evaluation is critical



Aktüel Tıp Derg 2000;5: 44-8

### PREGNANT DIALYSIS PATIENT

- Outcome also determined by comorbidities HTN, DNP
- Successful outcome rates?
  - on HD pre-conception 50%
  - initiating dialysis after conception 80%



#### **PREGNANT DIALYSIS PATIENT**

**Major risk factors :** 

- Age of the mother
- Primary kidney disease
- Dialysis duration before pregnancy
- Pregnancy week at dialysis initiation
- Dialysis type
- Hemoglobin during pregnancy
- Serum creatinine level
- Blood pressure
- Frequency of dialysis



# **PREGNANT DIALYSIS PATIENT**

# **Contemporary** series

Year	Region	Terminations	Losses	Live Birthe
2009	Japan		36%	64%
2014	Australia		27%	73%
2014	Canada		13.6	86.4%
2018	France	-	22%	78%
2018	Brazil		10.8%	89.2%
2019	USA	7.6%	32%	27%, but unknown 31%





Fig. 2. Dialysis prescription provided to pregnant HD patients.



Clinical Kidney Journal, 2017, vol. 10, no. 2, 276–281

# **MATERNAL COMPLICATIONS**

- Polyhydroamnios 47.3%
- Premature birth
- Preeclampsia
- Spontaneous abortion
- Maternal hypertension 56%
- Ablatio plasenta
- Cerebrovascular events

Adv Chronic Kidney Dis 2013;20(5):411-8 www.turkhipertansiyon.org/kongre2009/pdf/14\_mayıs/cengiz\_utaş.pdf www.tihudum.org/tihud\_content/uploods/ossets/5.38pdf



# **MATERNAL COMPLICATIONS**

- 14-44 years old HD female patients
- One year survival on dialysis is 90%
- Risk of death for dialysis pt who

becomes pregnant is not increased by

#### the pregnancy

Adv Chronic Kidney Dis 2013;20(5):411-8



# **FETAL COMPLICATIONS**

**Perinatal deaths 14.1%** 

- Prematurity is seen in 80%
- The mean age of pregnancy at delivery is 32 weeks
- Birth-weights of the infants <2,000 g



#### Dialysis

Women receiving maintenance dialysis before pregnancy Guideline 5.2.1

We recommend women established on dialysis prior to pregnancy receive pre-pregnancy counselling including the options of postponing pregnancy until transplantation (when feasible) and the need for long frequent dialysis prior to and during pregnancy (1C).

#### Guideline 5.2.2

We recommend women established on haemodialysis prior to pregnancy receive long, frequent haemodialysis either in-centre or at home to improve pregnancy outcomes (1C).

#### Guideline 5.2.3

We suggest women receiving haemodialysis during pregnancy have dialysis dose prescribed accounting for residual renal function, aiming for a pre-dialysis urea < 12.5 mmol/l (2C).

#### Guideline 5.2.4

We recommend women established on peritoneal dialysis prior to pregnancy should convert to haemodialysis during pregnancy (1D).

- Frequent Dx (5-7 days/week)
- BUN ≤50 mg/dl
- Low dose heparin and slow UF
- Sufficient calories and protein (0.8 gr/kg+20 gr/day) intake
- Vitamin replacement



Am J Kidney Dis 766-773, 1998

- BP control (metyldopa, labetalol, nifedipine)
- ACE-i, ARB, diuretics should not be prescribed
- DBP target at 80-90 mmHg



- Treat anemia (Hb:10-11 gr/dl)
- Add iron and folic acid
- If needed increase ESA dose
- Avoid metabolic acidosis
- Avoid hypocalcemia
- Avoid post dx hypercalcemia



# **DIALYSIS AND FETAL OUTCOME**

• In the largest study to date, the Registry for

**Pregnancy in Dialysis Patients reported a** 

significant correlation between hours spent on

dialysis therapy and improved fetal outcome.



### **DIALYSIS AND FETAL OUTCOME**





# **DIALYSIS AND FETAL OUTCOME**

- The increase in dialysis time seems to improve the pregnancy outcome and offer several advantages:
  - It ensures less uremic environment to the fetus and allows the mother more liberal diet (Potassium and protein)
  - It may help to control hypertension and fluid intake and may also reduce the amplitude of blood volume and electrolyte shifts





- BUN < 50 mg/dl WHY???
- 1963
  - 150 female CKD patients (no dx)
  - BUN is the only and most important parameter in fetal outcome
  - Fetal mortality directly linked to BUN



- No randomized prospective trials of pregnant women
- Only retrospective data
  - 16-20<sup>th</sup> week of pregnancy
  - Predialysis BUN ≤ 50 mg/dl
- 16–24 hours HD/week
  - High urea and fluid overload and polyhidramniosis
  - Less dialysis hypotension
  - More liberal diet

Journal of Medical Case Reports 2:10, 2008



# **Toronto USA Comparison**

The Toronto Pregnancy and Kidney Disease (PreKid) Registry

- N=22
- 18 established ESRD patients
- 4 approaching ESRD

The American Registry for Pregnancy in Dialysis Patients

- N= 70
- 57 established ESRD patients
- 13 approaching ESRD

#### Hladunewich JASN 2014

Pregnancy Outcomes			
Live Birth Rate Game C.	Ioronto	USA	PUblic
1" Trimester I	19 (86%)	43 (62%)	0.030
2nd Trimanter Loss	1 (5%)	5 (7%)	0.030
Nametal D. d	0 (0%)	14 (20%)	
Coll Dia	1 (5%)	5 (7%)	
Soul Birth	1.0%	3 (4%)	
Live Birth Rate (ESRD only)	15 (83%)	30 (53%)	0.030
Among Patients with Established I	ESRD	an grand	0.020
Dialysis Time (Hours/Week)	43±6	1745	
Gestational Age (Weeks)	36 (32-37)	27/01.20	-0.001
Among Patients with Renal Failus	e During Press	(48/2)	0.002
Dialysis Time (Hours/Week)	334	1544	-0.001
Gestational Age (Weeks)	35 (29-37)	33 (31.37)	-0.001
All Pregnancies (Except 1" and 24	Trimener Lours)	33(31-31)	0.5
Dialysis Time (Hours/Week)	47+7	1745	-0.001
Birth Weight (grams)	2118+857	1748+040	NE
Among Surviving Infants in Fete	blished ESPD I	atients	143
Normal Birth Weight	8 (50%)	10 (32%)	MC
Low Birth Weight (C)(00-)	7 (44*()	13 (304/)	103
New Low Dick Weight (~2500g)	1 (4474)	0.(39%)	
very Low Burn weight (<1500g)	1 (02*)	A (72.19)	

- Dialysate calcium (3 meq/l)
  - Hypocalcemia and/or post dx hypercalcemia

- Plasenta turns 25-hydroxy vitamin D3 to 1,25dihydroxy vitamin D3
- The need for Vitamin D throughout pregnancy
  - Vitamin D, parathormon, serum level of calcium and phosporus

EDNTDA-ERCA J 28(2): 91-94, 2002 Journal of Medical Case Reports 2: 10, 2008



ο.

Hemodialysis International 2005; 9: 147-152

#### Phosphorus-enriched hemodialysis during pregnancy: Two case reports

Syed HUSSAIN, Virginia SAVIN, Walter PIERING, Jane TOMASI, Samuel BLUMENTHAL Department of Medicine, Division of Nephrology, Medical College of Wisconsin, Milwaukee, Wisconsin, U.S.A.

**Figure 1** Pre- and post HD serum inorganic phosphate levels in the two patients reported. (Left, Case 1) Serum inorganic phosphate levels during the last 5 weeks of the reported patient's pregnancy. ( $\blacktriangle$ ) Before dialysis; (O) after dialysis. (Right, Case 2) Pre- ( $\blacklozenge$ ) and post-HD (O) phosphate levels starting from dialysis initiation through pregnancy termination. Time at which pregnancy was discovered and daily HD begun, as well as time at which inorganic phosphate was supplemented, is indicated. In both cases bicarbonate bath was supplemented with 90 mmol of inorganic phosphate, as described in the text.

#### Extra 3.66 mg/dL phosphorus added to the dialysate

Hemodialysis International 9: 147–152, 2005



- Erythropoietin can safely be administered
- Target hemoglobin is 10–11 g/dl
- Increase EPO dose by 50%
  - Increased vascular volume and hemodilution
  - Resistance to EPO (increased cytokine production)



EDNTDA-ERCA J 28(2): 91-94, 2002

Journal of Medical Case Reports 2: 10, 2008

- Introvenous iron and heparin are safe
- Frequent check for iron stores
- Minimal heparin dose

EDNTDA-ERCA J 28(2): 91-94, 2002

Journal of Medical Case Reports 2: 10, 2008



The first case of female pregnancy while on PD was reported in 1980s

The rates of conception in women on PD are going up but still relatively lower than the rates in women on HD

According to data collection from 1699, in childbearing-age women on PD, conception rate is only 1.1%



Am J Kidney Dis 1998;31:766–773.

#### Case Report

#### Successful Pregnancy in a 31-Year-Old Peritoneal Dialysis Patient with Bilateral Nephrectomy

#### Ahmed Abu-Zaid,<sup>1</sup> Ahmed Nazer,<sup>2</sup> Osama AlOmar,<sup>2</sup> and Ismail A. Al-Badawi<sup>2</sup>

 <sup>1</sup> College of Medicine, Alfaisal University, P.O. Box 50927, Riyadh 11533, Saudi Arabia
 <sup>2</sup> Department of Obstetrics and Gynecology, King Faisal Specialist Hospital and Research Center (KFSH & RC), P.O. Box 3354, Riyadh 11211, Saudi Arabia

At 29 weeks of gestation, mother developed severe episodes of hypertension (despite the aggressive antihypertensive medications) along with severe proteinuria (more than +3). A diagnosis of preeclampsia was made

> Cesarean section was uneventful and delivered a preterm baby girl, weighed 780 g, with Apgar score of 5, 7, and 7 at 1, 5, and 10 minutes, respectively

NEPHROLOGY 2008; 13, 380–383

doi:10.1111/j.1440-1797.2008.00938.x

#### Original Article

#### Peritoneal dialysis in pregnancy: A case series

#### ANDREW JEFFERYS,<sup>1</sup> KATE WYBURN,<sup>2</sup> JOSEPHINE CHOW,<sup>1</sup> BRUCE CLELAND<sup>1</sup> and ANNEMARIE HENNESSY<sup>2</sup>

<sup>1</sup>Department of Nephrology, Liverpool Hospital and <sup>2</sup>Department of Nephrology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

**SUMMARY:** Patients with significant renal impairment have difficulties maintaining a viable pregnancy due to maternal and fetal complications. Both peritoneal dialysis and hemodialysis support throughout pregnancy has been reported to assist in these pregnancies. We report our experience with the use of peritoneal dialysis in five cases leading to successful deliveries with minimal complications.



Experience over 10 years of two teaching hospitals in Sydney, Australia, with PD for significant renal impairment in pregnancy

5 patients were commenced on dialysis during pregnancy

Table 1 Complications and outcomes				
CAPD	Case	N = 5		
Maternal complications				
Exit site infection	Cases 1, 3, 5	3		
Malposition	Case 5	1		
Peritonitis	Case 1	1		
Worsening hypertension	Cases 1, 2	2		
Pre-eclampsia	Case 2	1		
Caesarean section	Cases 2, 4	2		
Obstetric complications				
Prematurity	Cases 1, 2, 3	3		
Polyhydramnios		0		

CADD another and data a setting of distance



# **GYN&OBS FOLLOW-UP**

- Use USG for pregnancy stage determination
- Check for urinary abnormalities (eg obstructive uropathy)
- Monthy USG after 28 weeks
- Beware of vaginal and urinary bacterial infections



#### **GYN&OBS FOLLOW-UP**

#### 25 weeks forward

- Close follow up of BP
- Evaluation of uterine and umbilical arteries perfusion
- Monitor pre-, inter- and post- HD fetal heart rate



#### LABOR

- Gyn&Obs follow-up
  - If not a necessity, then labor at term
  - Secarian section is only must with

obstetric causes



- 1980 survival of infants 20-30%
- 2003 survival of infants 50%
- Multidisciplinary approach
  - Patients
  - Nephrologists
  - Dialysis team
  - Gynecologists
  - Neonatologists





- 67% premature birth
- 37% IUGR
- 94% birth weight < 2500 g
- Neonatal death 10%



Nephrol Dial Transplant (2014) 29: 1578–1586 doi: 10.1093/ndt/gfu092 Advance Access publication 22 April 2014



#### **Original** Article

The children of dialysis: live-born babies from on-dialysis mothers in Italy—an epidemiological perspective comparing dialysis, kidney transplantation and the overall population

Giorgina Barbara Piccoli<sup>1</sup>, Gianfranca Cabiddu<sup>2</sup>, Giuseppe Daidone<sup>3</sup>, Gabriella Guzzo<sup>1</sup>, Stefania Maxia<sup>2</sup>, Ida Ciniglio<sup>1</sup>, Valentina Postorino<sup>4</sup>, Valentina Loi<sup>2</sup>, Sara Ghiotto<sup>1</sup>, Michele Nichelatti<sup>5</sup>, Rossella Attini<sup>6</sup>, Alessandra Coscia<sup>6</sup>, Maurizio Postorino<sup>7</sup> and Antonello Pani<sup>2</sup>, on behalf of the Italian Study Group "Kidney and Pregnancy"\*

<sup>1</sup>Department of Clinical and Biological Sciences, SS Nephrology, University of Torino, Italy, <sup>2</sup>Brotzu Hospital, SCD Nephrology, Cagliari, Italy, <sup>3</sup>Siracusa Hospital, SCD Nephrology, Siracusa, Italy, <sup>4</sup>Department of Neuroscience, Child Neuropsychiatry Unit, Bambino Gesù Children's Hospital, Rome, Italy, <sup>5</sup>Department of Oncology, Niguarda Hospital, Milano, Italy, <sup>6</sup>Department of Surgical Sciences, sant'Anna Hospital, University of Turin, Italy and <sup>7</sup>CNR-IBIM, Clinical Epidemiology and Physiopathology of Renal Diseases and Hypertension, Reggio Calabria, Italy



- ✓ Italy
- ✓ 23 (20 HD, 3 PD) patients
  ✓ 2000-2012

✓ 33.3% <34 weeks (mean 30 weeks)</li>
 ✓ 33.3% IUGR
 ✓ Mean birth weight 1200 gr



Nephrol Dial Transplant (2012) 27: 2365–2369 doi: 10.1093/ndt/gfr617 Advance Access publication 9 November 2011

# What about the renal function during childhood of children born from dialysed mothers?

Pauline Abou-Jaoude<sup>1</sup>, Laurence Dubourg<sup>2,3</sup>, Lucie Bessenay<sup>4</sup>, Adeline Pinçon<sup>1</sup>, Anne Jolivot<sup>5</sup>, Fitsum Guebre-Egziabher<sup>5</sup>, Pierre Cochat<sup>1,2,3</sup> and Justine Bacchetta<sup>1,2,3</sup>

<sup>1</sup>Service de Néphrologie et Rhumatologie Pédiatriques, Centre de Référence des Maladies Rénales Rares, Hôpital Femme Mère Enfant, Bron, France, <sup>2</sup>Service d'Explorations Fonctionnelles Rénales et Métaboliques, Hôpital Edouard Herriot, Lyon, France, <sup>3</sup>Université de Lyon, Lyon, France, <sup>4</sup>Service de Pédiatrie, CHU de Clermont Ferrand, Clermont-Ferrand, France and <sup>5</sup>Service de Néphrologie, Hôpital Edouard Herriot, Lyon, France



- ✓ Lyon, France
- ✓ 7 patients 10 pregnancies
- ✓ 2009
- ✓ Mean age at pregnancy 32 (29-39) weeks
- ✓ 7 premature babies
- ✓ Mean birth weight 1735 (930-3430) gr
- ✓ Mean height 42 (35-51) cm
- ✓ 7 babies in neonatal care
  - ✓ 5 mechanical ventilation





#### **BRENNER HYPOTHESIS**

'Individuals with a congenital reduction in

nephron number have a much greater likelihood

of developing adult hypertension and

subsequent renal failure.'



Am J Hypertens 1998: 1:335-47

#### **BARKER HYPOTHESIS**

'Intrauterine growth retardation, low birth weight, and premature birth have a causal relationship to the origins of hypertension, coronary heart disease, and non-insulindependent diabetes, in middle age.'



- ✓ Renal function tests at 4.5 years
- ✓ None had HT
- ✓ Mean BP 65/35 mmHg
- ✓ GFH 129 ml/min (according to Schwartz)
- ✓ Inuline clearence 138 ml/min





# **IN SUMMARY**

- During Pregnancy
  - Duration
  - Adequacy
  - Nutrition

Follow up closely!

- Anemia
- Calcium and phosphorus
- Dry weight
- Blood pressure



#### **IN SUMMARY**

• Follow-up of a pregnant dialysis patient

should be multidisciplinary

Fertile female patients should be informed

about chances of conception and advisable

methods for protection





#### THANK YOU FOR YOUR KIND INTEREST