Sistema Socio Sanitario

Regione Lombardia

Fondazione IRCCS Policlinico San Matteo

ATS Pavia

GRAND ROUNDS CLINICI DEL MERCOLEDÌ
con il Policlinico San Matteo

Aula Magna "C. Golgi" & WEBINAR

10 Aprile 2024

Gravidanza ad alto rischio: trapianto di rene

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SC Ostetricia e Ginecologia 1

E.F

38 anni

Riscontro di ipertensione arteriosa durante l'adolescenza

A 16 anni ESKD secondaria a ipoplasia renale bilaterale misconosciuta --> trattamento emodialitico

12/1999 trapianto di rene da donatore cadavere

2001 sospetto di rigetto acuto trattato con boli di metilprednisolone

Dal 2012 funzione renale stabile (creatininemia 1.6 mg/dl eGFR 40-45 ml/min per 1.73m^2)

Ipertensione arteriosa cronica in trattamento con ACE inibitore

2016 1G (follow

A 16 s omparsa di proteinuria >1g/24h

Abort

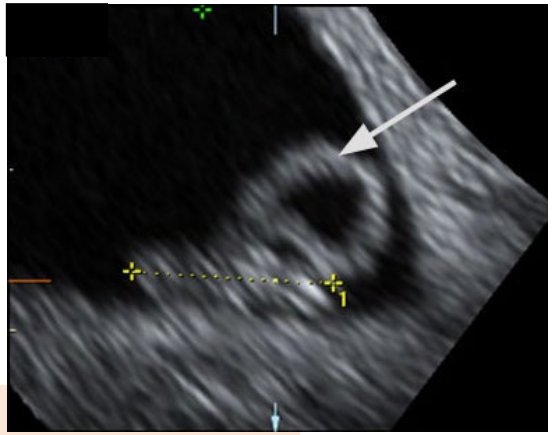
GFR categories (ml/min/1.73 m²) Description and range		
G1	Normal or high	≥90
G2	Mildly decreased	60–89
G3a	Mildly to moderately decreased	45–59
G3b	Moderately to severely decreased	30–44
G4	Severely decreased	15–29
G5	Kidney failure	<15

Gozzo multinodulare non tossico

2017 e 2018 IV

2019 creatinina 1.99 mg/dl eGFR 31 ml/min per 1.73m^2, assenza di proteinuria

I visita 10/2020 Ambulatorio gravidanza ad alto rischio



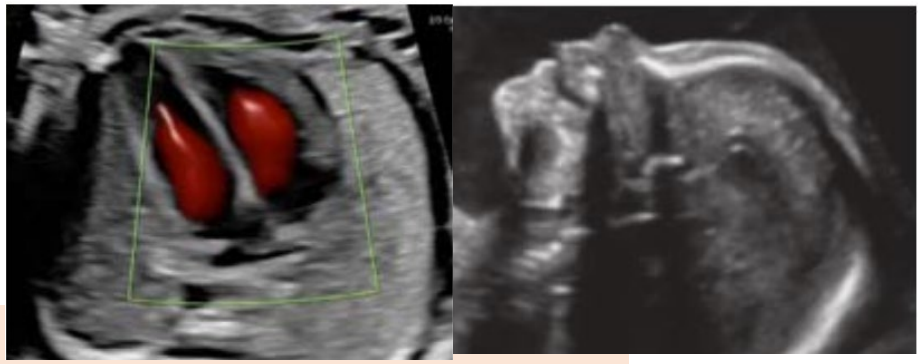
6 settimane

Gravidanza	Esami	Terapia
Peso materno 59 kg	Creatininemia 1.46 mg/dl eGFR 41.7 ml/min per 1.73m^2	Azatioprina 50mg/die
CRL 4 mm corrispondente BCE presente	Proteinuria 0,24 g/24h	Ciclosporina 60 mg x2
	Hb 10.5 g/dl	Metilprednisolone 4 mg/die
		Metildopa 250 mg x2 (ACE inibitore sospeso alla 6^ settimana)
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
		Colecalciferolo 2000 UI/die

12 settimane

Gravidanza	Esami	Terapia
Peso materno 57 kg (-2 kg)	Creatininemia 1.3mg/dl eGFR 50 ml/min per 1.73m^2	Azatioprina 50mg/die
Screening I trimestre: Basso rischio trisomie Alto rischio preeclampsia >34 wks	Proteinuria 0.65 g/24h	Ciclosporina 70 mg x2
	Acido urico 9 mg/dl	Metilprednisolone 4 mg/die
	Hb 11.7 g/dl	Acido acetil salicilico 150 mg/die
	PCR 0.3 5mg/dl	Metildopa 250 mg x2
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
	25OH vit D 16 ng/ml	Colecalciferolo 2000 UI/die

21 settimane



Gravidanza	Esami	Terapia
Peso materno 57 kg (stabile rispetto al precedente)	Creatininemia 1.5 mg/dl eGFR 43.7 ml/min per 1.73m^2	Azatioprina 50 mg/die
Ecografia ostetrica 20 settimane Anatomia fetale nella norma Biometria fetale percentili medi	Proteinuria 0.8 g/24h	Ciclosporina 80 mg x2
	Acido urico 8 mg/dl	Metilprednisolone 4 mg/die
	Hb 10.4g/dl	Acido acetil salicilico 150 mg/die
	PCR 0,35 mg/dl	Metildopa 250 + 250 + 500 mg
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
	25OH vit D 25 ng/ml	Colecalciferolo 2000 UI/die

26 settimane

Gravidanza	Esami	Terapia
Peso materno kg 58.5 (-0.5 kg)	Creatininemia 1.6 mg/dl eGFR 40 ml/min per 1.73m^2	Azatioprina 50 mg/die
Ecografia ostetrica 26 settimane Crescita fetale regolare Biometria fetale percentili medi	Proteinuria 2.27 g/24h	Ciclosporina 80 mg x2
Monitoraggio pressorio domiciliare <130/80 mmHg	Acido urico 7.7 mg/dl	Metilprednisolone 4 mg/die
Ecografia renale: regolare vascolarizzazione del rene trapiantato in FID	Hb 10.3g/dl	Acido acetil salicilico 150 mg/die
	PCR 0,68 mg/dl	Metildopa 250 + 250 + 500 mg
	OGTT negativa	Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
	25OH vit D 25 ng/ml	Colecalciferolo 2000 UI/die

30 settimane

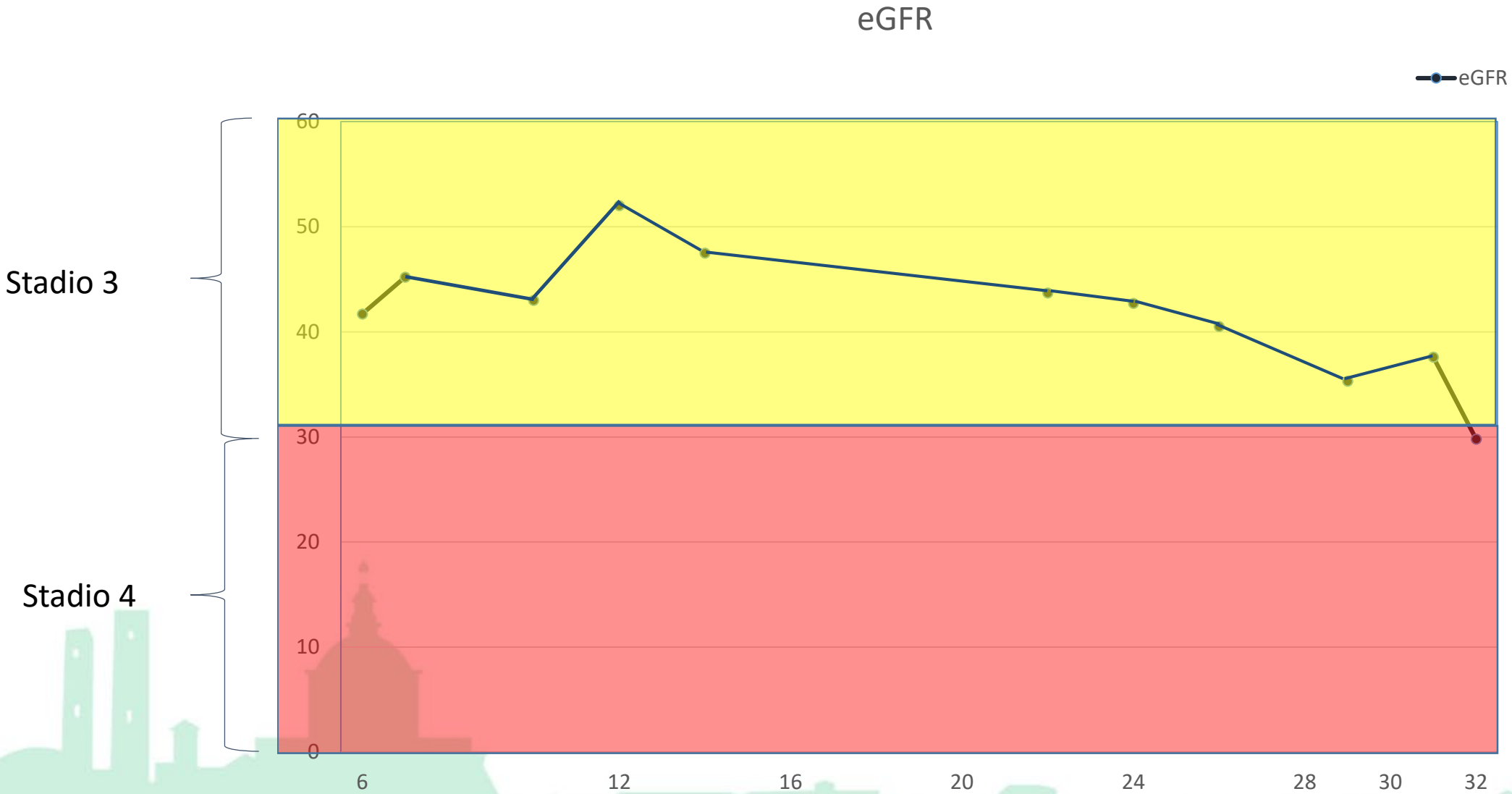
Gravidanza	Esami	Terapia
Peso materno kg 58.5 (stabile rispetto al precedente)	Creatininemia 1.75 mg/dl eGFR 36.3 ml/min per 1.73m^2	Azatioprina 50 mg/die
Ecografia ostetrica 30 settimane Crescita fetale regolare Biometria percentili medi PP podalica	Proteinuria 1.79 g/24h	Ciclosporina 80 mg x2
Monitoraggio pressorio domiciliare <130/80 mmHg	Acido urico 9.2 mg/dl	Metilprednisolone 4 mg/die
	Hb 9.9 g/dl	Acido acetil salicilico 150 mg/die
	PCR 0.4 mg/dl	Metildopa 250 + 250 + 500 mg
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
	25OH vit D 27 ng/ml	Colecalciferolo 2000 UI/die

31 settimane

Gravidanza	Esami	Terapia
Peso materno kg 58.5 (stabile rispetto al precedente)	Creatininemia 1.7 mg/dl eGFR 36.3 ml/min per 1.73m^2	Azatioprina 50 mg/die
Ecografia ostetrica Liquido amniotico regolare Flussi regolari PP podalica	Proteinuria 2.7 g/24h	Ciclosporina 80 mg x2
Monitoraggio pressorio domiciliare <130/80 mmHg	Acido urico 8.4 mg/dl	Metilprednisolone 4 mg/die
Ecografia renale: regolare vascolarizzazione del rene trapiantato in FID	Hb 9.9 g/dl	Acido acetil salicilico 150 mg/die
	PCR 0.4 mg/dl	Metildopa 250 + 250 + 500 mg
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
	25OH vit D 35 ng/ml	Colecalciferolo 2000 UI/die

32 settimane + 4 giorni

Gravidanza	Esami	Terapia
Peso materno kg 58.5 (stabile rispetto al precedente)	Creatininemia 2.08 mg/dl eGFR 29 ml/min per 1.73m^2	Azatioprina 50 mg/die
Ecografia ostetrica 30 settimane Crescita fetale regolare Biometria percentili medi PP podalica	Proteinuria 4 g/24h	Ciclosporina 80 mg x2
Monitoraggio pressorio domiciliare <130/80 mmHg	Acido urico 9.4 mg/dl	Metilprednisolone 4 mg/die
	Hb 9.7 g/dl	Acido acetil salicilico 150 mg/die
		Metildopa 250 + 250 + 500 mg
		Eritropoietina 150 mcg ogni 30 gg
		Omeprazolo 20 mg/die
		Colecalciferolo 2000 UI/die



- 23/04/2021 ricovero presso OUC Ostetricia e Ginecologia per peggioramento della funzionalità renale

- 23-24/04 profilassi RDS
- 25/04 taglio cesareo in urgenza a 32 settimane + 6 giorni per attività contrattile in PP podalica

Nasce Elisa 1690 g (AGA)

Apgar 1’ 8 -5’ 9

pH cordonale arterioso 7.27 BE -6

Postpartum

	Esami	Terapia alla dimissione
Inibizione della galattopoiesi con cabergolina	Creatininemia 1.7 mg/dl eGFR 37 ml/min per 1.73m^2	Azatioprina 50 mg/die
	Proteinuria 4.4 g/24h	Ciclosporina 70 mg x2
	Acido urico 8 mg/dl	Metilprednisolone 4 mg/die
	Hb 10.1 g/dl	Amlodipina 5mg 1 cp/die
		Labetalolo 100 mg cp x2
		Ramipril 5mg 1 cp x 2
		Eritropoietina beta 5000 UI per 3 volte alla settimana
		Omeprazolo 20 mg/die

Oggi

Terapia
Azatioprina 50 mg/die
Ciclosporina 70 mg x2
Metilprednisolone 4 mg/die
Labetalolo 100 mg/die
Ramipril 5mg 1 cp x 2
Metossipolietileglicole-epoetina beta 200 mcg 1 fiala sc ogni 28 giorni
Omeprazolo 20 mg/die
Calcitriolo 0.25 mcg/die

07/2021 creatinina 2.34 mg/dl (eGFR 25 ml/min per 1.73m2)

03/22 Ecografia renale:

- *rene trapiantato in fossa iliaca destra, margini e dimensioni regolari (circa 12 cm), parenchima normoecogeno e di spessore conservato, differenziazione corticomidollare*
- *Non visibili calcoli, permane modesta dilatazione della pelvi. Vescica ben distesa con pareti regolari, contenuto limpido anecogeno senza calcoli nel lume né vegetazioni di parete.*
- *Vascolarizzazione intrarenale è uniforme e ben sviluppata con Indici di Resistenza delle arteriole intraparenchimali ampiamente nei limiti della norma,*
- *Vena renale pervia senza segni di trombosi.*
- *Non stenosi dell'arteria renale*

02/2024 creatinina 1,96 (eGFR 31 ml/min per 1.73m^2) controllo pressorio ottimale funzionalità renale stabile

Gravidanza 6 settimane **CKD stadio 3**…

… gravidanza 32+4 settimane **CKD stadio 4**

Table 2. Renal and Pregnancy Outcomes According to Chronic Kidney Disease Stage

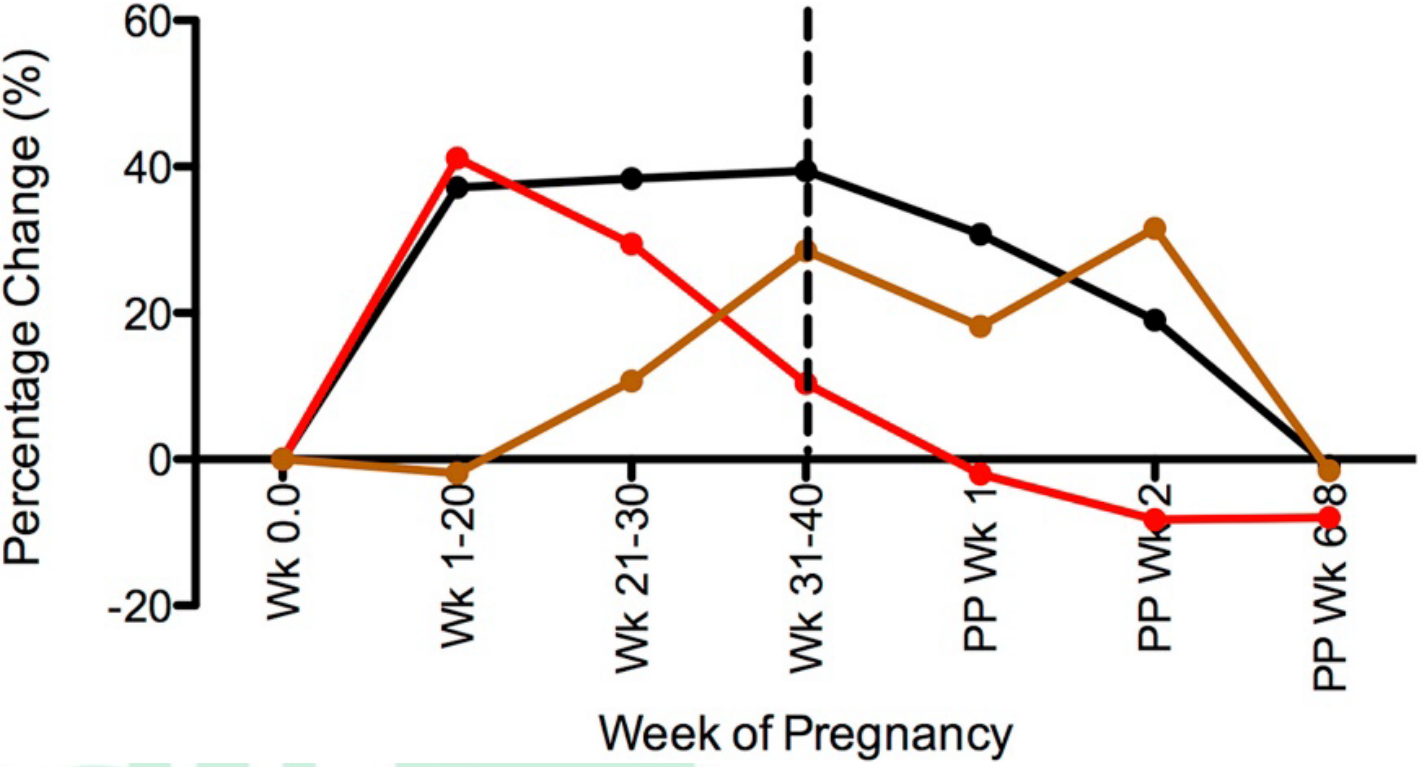
Outcome	Control Group (n=836)	Stage 1 (n=370)	Stage 2 (n=87)	Stage 3 (n=37)	Stage 4–5 (n=10)
Progressed to next stage of CKD	NA	7.6	12.6	16.2	20
New-onset HTN	5.5	7.9	17.6	47.1	50
New-onset or doubling of proteinuria	NA	20.5	37.9	86.5	70

CKD, chronic kidney disease; NA, not applicable; HTN, hypertension; SGA, small for gestational age; NICU, neonatal intensive care unit.
Data are % or mean±SD.
Data from Piccoli GB, Cabiddu G2, Attini R3, Vigotti FN4, Maxia S2, Lepori N, et al. Risk of adverse pregnancy outcomes in women with CKD. J Am Soc Nephrol 2015;26:2011-22.

Hui D, Hladunewich MA. Chronic Kidney Disease and Pregnancy. Obstet Gynecol. 2019

Gravidanza 6 settimane **eGFR** 41.7 ml/min per 1.73m^2…

…Gravidanza 32+4 settimane **eGFR** 29 ml/min per 1.73m^2



$$GFR = \kappa_f \times (\Delta P - \pi_{GC})$$

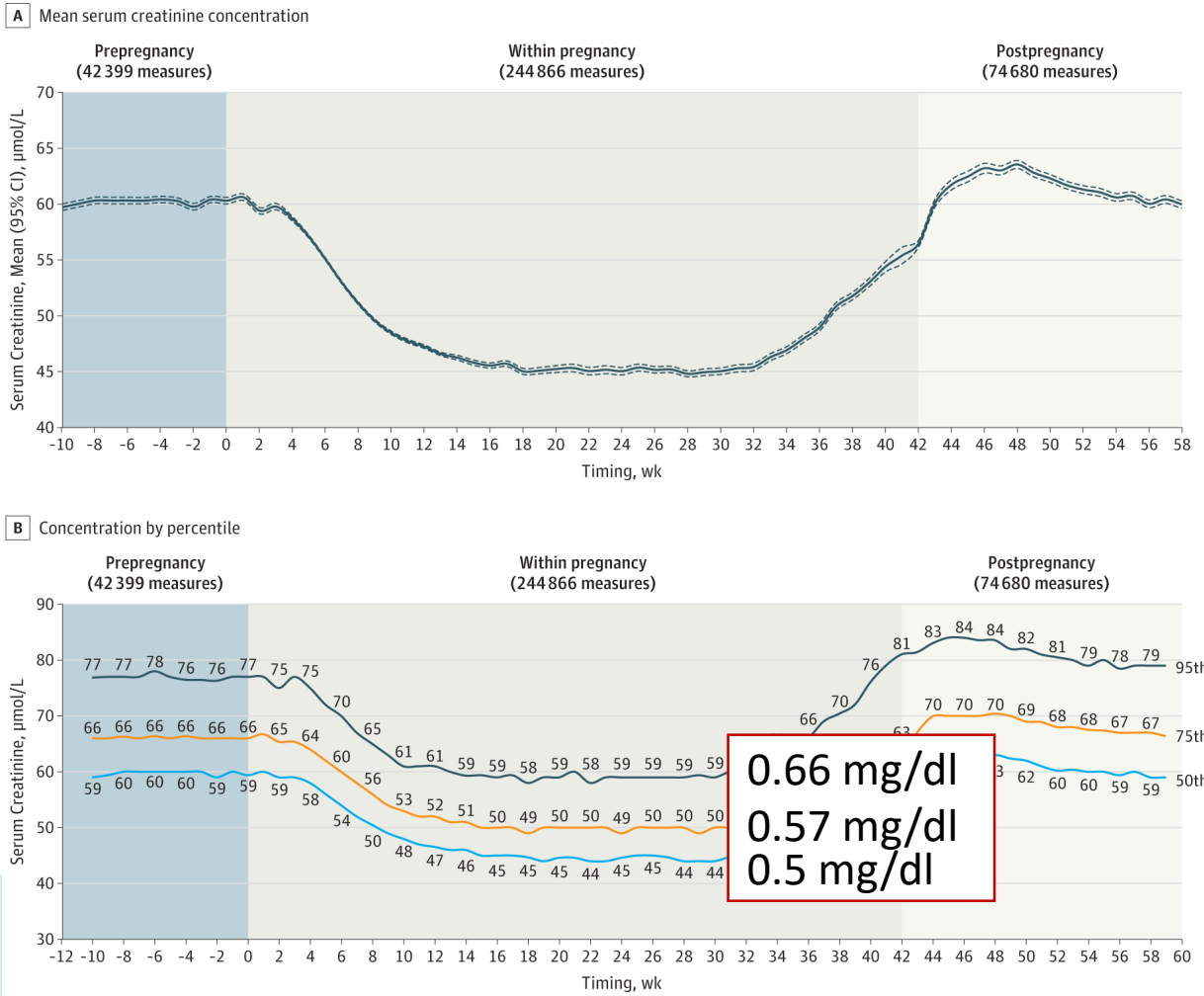
ΔP pressione idraulica transcapillare
π_{GC} pressione oncotica
K_f coefficient di ultrafiltrazione glomerulare (superficie disponibile per la filtrazione e la permeabilità dei 3 strati glomerulari)

Escrezione urinaria di proteine (significativa >300 mg/24h)

Hladunewich MA. Chronic Kidney Disease and Pregnancy. Semin Nephrol. 2017

Gravidanza 6 settimane **creatinina sierica** 1,46 mg/dl…

…Gravidanza 32+4 settimane **creatinina sierica** 2,08 mg/dl



0.88 mg/dl
0.75 mg/dl
0.67 mg/dl

0.66 mg/dl
0.57 mg/dl
0.5 mg/dl

0.9 mg/dl
0.76 mg/dl
0.67 mg/dl

Harel Z et al. Serum Creatinine Levels Before, During, and After Pregnancy. JAMA. 2019

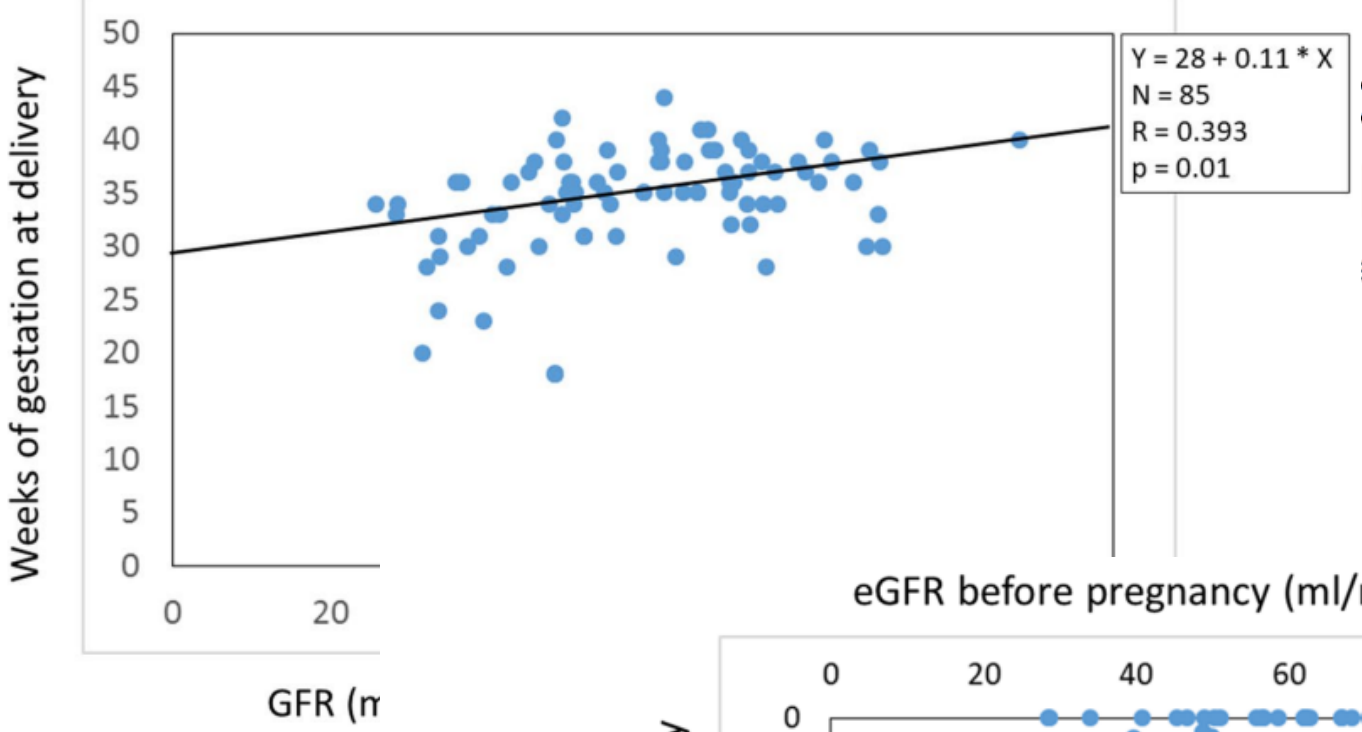


Fig. 1 Estimated GFR before pregnancy was corre

d pregnancy outcomes plantation

a Einecke[1], Frieder Keller[2], Ulrike Bode[3], Hermann Haller[1] and

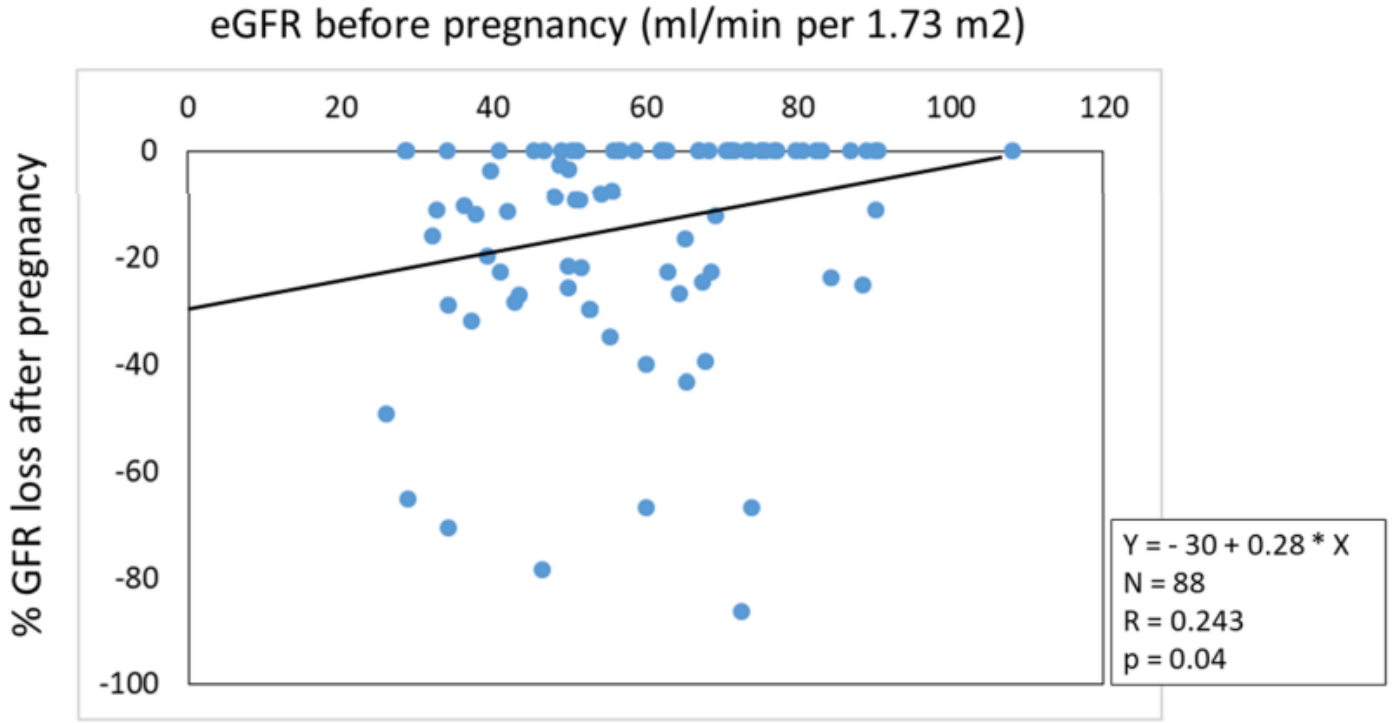


Fig. 2 Estimated GFR (eGFR) before pregnancy was correlated with the percent loss of eGFR measured 3–4 months after pregnancy ($p = 0.04$)

Schwarz A et al. Graft function and pregnancy outcomes after kidney transplantation. BMC Nephrol. 2022

Gravidanza 6 settimane **eGFR** 41.7 ml/min per 1.73m^2…

…Gravidanza 32+4 settimane **eGFR** 29 ml/min per 1.73m^2

A nationwide Dutch cohort study shows relatively good pregnancy outcomes after kidney transplantation and finds risk factors for adverse outcomes

Margriet E. Gosselink[1], Marleen C. van Buren[2], Judith Kooiman[1], Henk Groen[3], Wessel Ganzevoort[4], Henk W. van Hamersvelt[5], Olivier W.H. van der Heijden[6], Jacqueline van de Wetering[2] and A. Titia Lely[1]

STUDY DESIGN & METHODS

Netherlands 1971-2017

Retrospective cohort KT:
- Pregnancy > 20 weeks
- Analyses per prepregnancy eGFR-CKD-category

Combined adverse pregnancy outcome (cAPO):
- Birthweight <2500 gram
- Preterm birth <37 weeks
- Severe hypertension
- >15% graft deterioration

Results (1)

Cohort: 288 pregnancies

- Live birth rate 93%
- Mean gestational age 35.6 weeks
- Mean birthweight 2383 gram

- Preterm birth 50%
- Gestational hypertension 26%
- Preeclampsia 34%
- Cesarean section 48%

Results (2)

Independent risk factors cAPO:
1. Prepregnancy eGFR *(OR 0.98 (95% CI 0.96–0.99)*
2. Midterm percentage SCr dip *(OR 0.95, 0.93-0.98)*
3. Midterm MAP dip *(OR 0.94, 0.90-0.98)*

- cAPO risk indicator for graft loss *(HR 2.55, 1.09-5.96)*
- No significant risk factor if corrected for prepregnancy eGFR *(HR 2.18, 0.92-5.13)*.

- Prepregnancy graft function and hemodynamic adaptation to pregnancy most important risk factors for adverse outcomes

Gosselink ME et al. A nationwide Dutch cohort study shows relatively good pregnancy outcomes after kidney transplantation and finds risk factors for adverse outcomes. Kidney Int. 2022

Patients with Stage 1 CKD	Cesarean Section	Preterm Delivery <34 wk	Preterm Delivery <37 wk	SGA Parazzini <10th	Need for NICU	Stage Shift (or RRT	Doubling of or New-Onset Proteinuria	General Combined Outcome	Severe Combined Outcome
All patients (*n*=370)									
Age (≥30 versus <30 yr)	0.95 (0.58 to 1.56)	0.99 (0.35 to 2.79)	1.48 (0.81 to 2.70)	1.44 (0.72 to 2.87)	1.32 (0.58 to 3.01)	2.11 (0.81 to 5.48)	1.25 (0.69 to 2.70)	1.45 (0.87 to 2.41)	1.29 (0.72 to 2.31)
Multi- versus nulliparous	0.78 (0.48 to 1.25)	0.51 (0.20 to 1.32)	0.93 (0.54 to 1.62)	0.64 (0.33 to 1.21)	0.82 (0.39 to 1.74)	0.90 (0.40 to 2.00)	0.90 (0.52 to 1.58)	0.90 (0.56 to 1.45)	0.74 (0.43 to 1.27)
Baseline hypertension	2.55 (1.38 to 4.70)	12.22 (4.45 to 33.60)	3.44 (1.89 to 6.26)	1.91 (0.93 to 3.96)	3.07 (1.39 to 6.76)	0.98 (0.38 to 2.54)	3.80 (2.03 to 7.11)	2.68 (1.53 to 4.72)	2.53 (1.37 to 4.67)
Baseline proteinuria ≥1 g/d	2.16 (0.94 to 4.96)	4.81 (1.48 to 15.66)	3.65 (1.61 to 8.24)	2.12 (0.84 to 5.36)	3.67 (1.43 to 9.41)	1.94 (0.61 to 6.15)	0.69 (0.25 to 1.89)	3.42 (1.55 to 7.57)	3.05 (1.38 to 6.75)
Systemic disease	3.20 (1.35 to 7.55)	1.70 (0.57 to 5.09)	3.16 (1.52 to 6.54)	0.90 (0.34 to 2.37)	2.00 (0.79 to 5.08)	1.51 (0.51 to 4.43)	3.33 (1.56 to 7.11)	2.38 (1.17 to 4.85)	1.45 (0.68 to 3.11)
P value (H&L)	0.89	0.56	0.79	0.84	0.29	0.13	0.95	0.75	0.59

Piccoli GB et al. Risk of Adverse Pregnancy Outcomes in Women with CKD. J Am Soc Nephrol. 2015

…Aspirina 150 mg/die

Risk level	Risk factors
High[b]	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Pregestational type 1 or 2 diabetes • Kidney disease • Autoimmune disease (ie, systemic lupus erythematous, antiphospholipid syndrome) • Combinations of multiple moderate-risk factors
Moderate[c]	• Nulliparity • Obesity (ie, body mass index >30) • Family history of preeclampsia (ie, mother or sister) • Black persons (due to social, rather than biological, factors)[d] • Lower income[d] • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, >10-year pregnancy interval) • In vitro conception
Low	Prior uncomplicated term delivery and absence of risk factors

Table 2 Maternal and fetal outcomes of patients with and without aspirin therapy during pregnancy

Characteristics	Stage 1–2 CKD			Stage 3–5 CKD		
	Aspirin	Without aspirin	*P*	Aspirin	Without aspirin	*P*
Cases	63	63		22	19	
Gestation weeks at delivery (weeks)	37.0 ± 2.5	37.8 ± 2.6	0.06	35.1 ± 3.3	34.3 ± 3.9	0.49
Average birth weight (g)	2864 ± 683	3076 ± 620	0.07	2406 ± 724	2234 ± 797	0.48
Adverse maternal outcomes						
Delivery by CS, n (%)	41 (65.1%)	31 (49.2%)	0.07	19 (86.4%)	16 (84.2%)	1.00
Chronic hypertension, n (%)	23 (36.5%)	8 (12.7%)	0.002*	14 (63.6%)	6 (31.6%)	0.04*
Gestational hypertension, n (%)	3 (4.8%)	7 (11.1%)	0.19	0	0	–
Preeclampsia, n (%)	19 (30.2%)	10 (15.9%)	0.06	4 (18.2%)	8 (42.1%)	0.09
Severe preeclampsia, n (%)	15 (23.8%)	8 (12.7%)	0.11	3 (13.6%)	8 (42.1%)	0.04*
Heart failure, n (%)	0	0	–	0	1 (5.3%)	0.46
eGFR decline > 30%, n (%) or ESRD	2 (3.2%)	2 (3.2%)	1.00	4 (18.2%)	6 (31.6%)	0.53
Adverse fetal outcomes						
Fetal death, n (%)	0	1 (1.6%)	1.00	1 (4.5%)	1 (5.3%)	1.00
Induced abortion, n (%)	0	1 (1.6%)	1.00	0	1 (5.3%)	0.46
Fetal–neonatal death, n (%)	0	0	–	1 (4.5%)	0	1.00
Preterm birth, n (%)	19 (30.2%)	10 (15.9%)	0.06	11 (50%)	12 (63.2%)	0.40
Before 34 weeks	9 (14.3%)	4 (6.3%)	0.14	4 (18.2%)	4 (21.1%)	1.00
34–37 weeks	10 (15.9%)	6 (9.5%)	0.29	7 (31.8%)	8 (42.1%)	0.50
FGR	2 (3.2%)	2 (3.2%)	1.00	0	0	–
NICU admission	11 (17.5%)	6 (9.5%)	0.19	7 (31.8%)	7 (36.8%)	0.74
Neonatal asphyxia	4 (6.3%)	4 (6.3%)	1.00	2 (9.1%)	2 (10.5%)	1.00
Respiratory distress syndrome	7 (11.1%)	4 (6.3%)	0.34	5 (22.7%)	4 (21.1%)	1.00
Intracranial hemorrhage	0	0	–	1 (4.5%)	0	1.00
Necrotizing enterocolitis	1 (1.6%)	0	1.00	1 (4.5%)	0	1.00

CS cesarean section, *eGFR* estimated glomerular filtration rate, *ESRD* end-stage renal disease, *FGR* fetal growth restriction, *NICU* neonatal intensive care unit

*$P < 0.05$

US Preventive Services Task Force; Davidson KW et al. Aspirin Use to Prevent Preeclampsia and Related Morbidity and Mortality: US Preventive Services Task Force Recommendation Statement. JAMA. 2021

Wang M et al. Low-dose aspirin for the prevention of severe preeclampsia in patients with chronic kidney disease: a retrospective study : This is the study for kidney and pregnancy.. J Nephrol. 2021

…Monitoraggio pressorio domiciliare <130/80 mmHg

Drug	Main features with respect to side effects in CKD	FDA "classic" labeling
Usually considered first choice drugs		
Alpha-methyl dopa	May not be able to correct severe hypertension in CKD. It is associated with autoimmune manifestations	B
Nifedipine	The side effect of peripheral edema may be more relevant in CKD patients and even more so in the presence of proteinuria	C
Labetalol	The side effects of dizziness and orthostatic hypotension may be particularly relevant in some CKD patients	C
Usually considered second choice drugs		
Beta blockers	Depression and fatigue may be particularly relevant in CKD patients. Bradycardia may be important, it may be a confounding factor in case of hyperkalemia, and tachycardia may appear after discontinuation	D atenolol B pindolole C metoprolol
Clonidine	Depression and fatigue may be particularly relevant in CKD patients. Hypertensive crises at discontinuation may mimic PE and may be severe even in case of the occasional "missed pill"	C
Alpha blockers	Orthostatic hypotension may be important, in particular in patients with baseline neurological impairment including diabetic nephropathy or SLE	C
Diuretics	See dedicated paragraph	B
To be avoided		
Short-acting nifedipine	Contraindicated by the FDA, RCOG, and AIPE due to the risk of severe hypotension with detrimental effects on placental flows. Severe sudden hypotension may have detrimental effects on kidney function	D
ACEi ARBs	Contraindicated due to the risk of major malformations, including cardiovascular, central nervous system, renal, and bone. These drugs are often implicated in AKI, and this may be particularly relevant in pregnant CKD patients	C 1st D 2nd 3rd

Piccoli GB et al. Hypertension in CKD Pregnancy: a Question of Cause and Effect (Cause or Effect? This Is the Question). Curr Hypertens Rep. 2016.

…Monitoraggio pressorio domiciliare <130/80 mmHg

Patients with known kidney disease and chronic hypertension referred by the nephrologist within the first 12 gestational weeks		
Well-controlled hypertension (only 1 drug) before pregnancy	Discontinue ACEi, ARBs, and diuretics and control blood pressure at least daily (better yet twice a day); there may not be a need for antihypertensive agents, at least in the first pregnancy stages. Strict home monitoring may also help identify when to resume treatment (usually in the 2nd trimester). A "late" BP rise may be an indication for hospitalization and/or delivery (depending on fetal status and gestational age)	<130/80
Well-controlled hypertension (2 or more drugs)	Same as above, but if discontinuing ACE or ARBs, start treatment with either alpha-methyldopa (our first choice) or nifedipine (second choice). Ask for at least twice daily BP control. 24-BP monitoring may be of help especially for detecting nocturnal hypertension; prescribed in particular cases	<130/80
Poorly controlled hypertension	Depending on the actual control, start treatment with either alpha-methyldopa at full doses (500 mg × 3 or × 4 daily) or with both alpha-methyldopa and nifedipine. Hospitalize in case of poor control, in particular in late CKD stages. 24-h BP monitoring at baseline and, as a general indication, each trimester. Other drugs (doxazosin or low dose diuretics) may be added in selected cases. Labetalol is not readily available in Italy and is usually a third choice due to logistic reasons. Involve the patient in strict home BP control (may be difficult if baseline poor control is linked to poor compliance)	Individualized; ideally slowly reaching <130/80

Piccoli GB et al. Hypertension in CKD Pregnancy: a Question of Cause and Effect (Cause or Effect? This Is the Question). Curr Hypertens Rep. 2016.

Usually considered as safe		
Azathioprine	This is the most widely used immunosuppressive drug. It is teratogen in animal models, but not in humans, possibly because the foetal liver is not able to activate the drug. KDIGO and European Best Practice Guidelines suggest switching from mycophenolate to azathioprine before pregnancy	D
Cyclosporine A	This calcineurin inhibitor has not been associated with increased teratogenicity; however, small for gestational age babies and preterm delivery have been reported, possibly due to the maternal disease and not specifically to the drug. Levels may vary in pregnancy and the hypertensive, hyperglycaemic and nephrotoxic effects should be mentioned	C
Tacrolimus	The drug has similar effects and side effects to cyclosporine A; experience is more limited than with the previous drug	C
Steroids	Together with azathioprine these are the most often employed and best known drugs. The most frequently used short-acting corticosteroids include prednisone, methylprednisolone and prednisolone, while betamethasone and dexamethasone are among the long-acting drugs. No ma have been reported, and the issue of labiopalatoschisis is debated. A higher risk of of membranes has been reported. Other relevant side effects include infectious risk risk of gestational diabetes	C
To be avoided		
Mycophenolate	Severe foetal malformations are reported, mainly involving cardiovascular and crani Discontinuation for at lest 6 weeks, to stabilize kidney function, is usually indicate transplantation	
m-Tor inhibitors	Very few studies have considered their use in pregnancy. They are teratogenic in ani tinuation in humans is a matter of debate. KDIGO guidelines suggest discontinuat of pregnancy	
Rituximab, simulect	Too few studies to allow safe use in pregnancy. Need for further evidence, but trials undertaken	

Terapia
Azatioprina 50 mg/die
Ciclosporina 80 mg x2
Metilprednisolone 4 mg/die

Terapia con agenti stimolanti eritropoietina

- alcune segnalazioni sparse hanno suggerito che la terapia con eritropoietina (EPO) può aumentare la pressione arteriosa nelle donne ipertese con CKD
- Esperienza clinica con gli ESA è in aumento e nel complesso rassicurante. I rischi sono probabilmente limitati e di gran lunga inferiori a quelli legati alle trasfusioni di sangue
- Patogenesi multifattoriale dell'anemia in gravidanza
- Target 10 g/dl

Piccoli GB et al. Hypertension in CKD Pregnancy: a Question of Cause and Effect (Cause or Effect? This Is the Question). Curr Hypertens Rep. 2016
Cabiddu G. et al. Kidney and Pregnancy Study Group of the Italian Society of Nephrology. A best-practice position statement on pregnancy after kidney transplantation: focusing on the unsolved questions. The Kidney and Pregnancy Study Group of the Italian Society of Nephrology. J Nephrol. 2018

Gravidanza 6 settimane proteinuria 0,24 g/24h…

… gravidanza 32+5 settimane proteinuria 4 g/24h

Pre-eclampsia*

De novo

Pre-eclampsia (de novo) is gestational hypertension accompanied by one or more of the following new-onset conditions at ≥20 weeks' gestation:

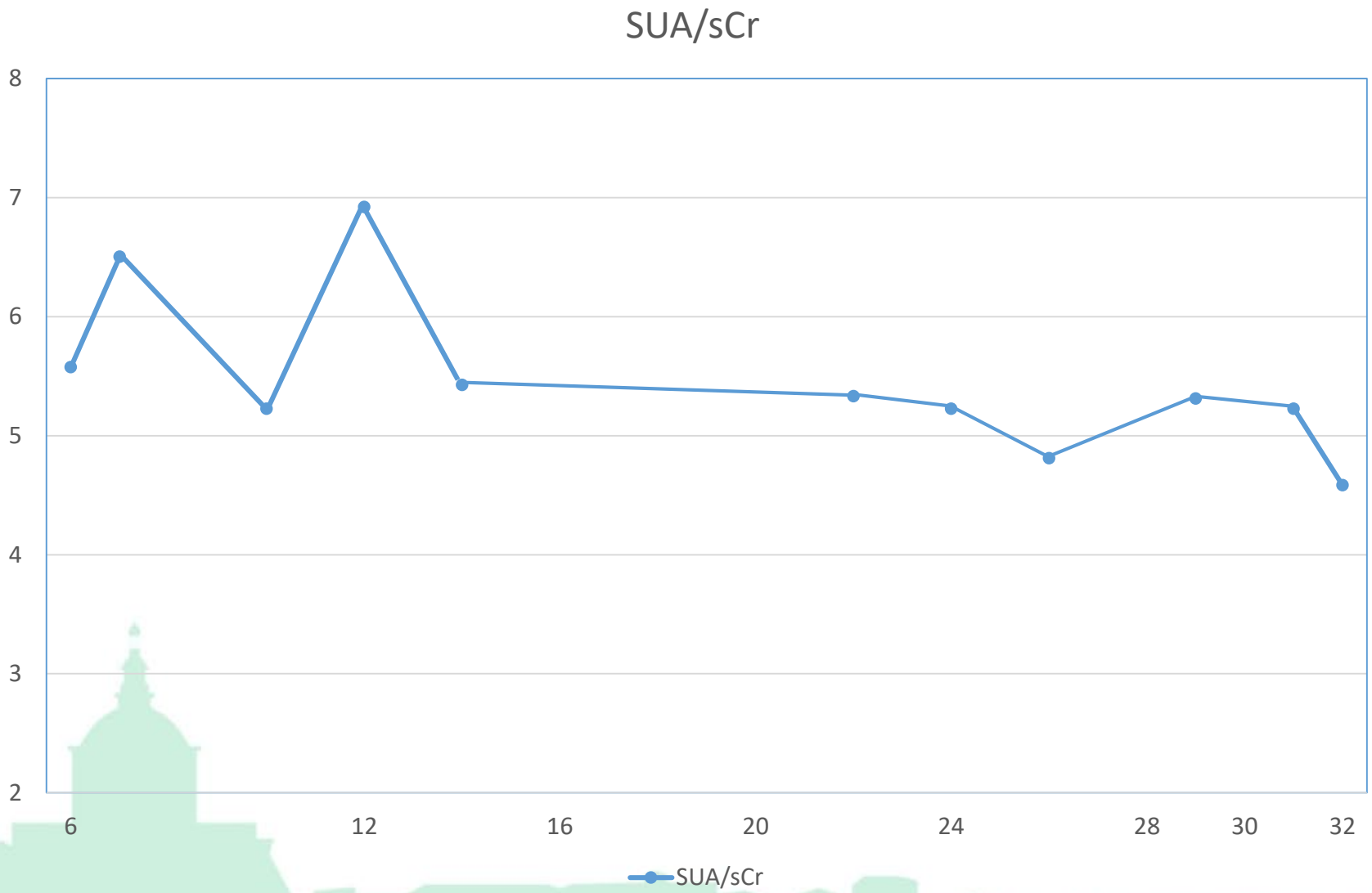
1. Proteinuria
2. Other maternal end-organ dysfunction, including:
   - Neurological complications (e.g., eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, or persistent visual scotomata)
   - Pulmonary oedema
   - Haematological complications (e.g., platelet count < 150,000/μL, DIC, haemolysis)
   - AKI (such as creatinine ≥ 90 μmol/L or 1 mg/dL)
   - Liver involvement (e.g., elevated transaminases such as ALT or AST > 40 IU/L) with or without right upper quadrant or epigastric abdominal pain)
3. Uteroplacental dysfunction (e.g., placental abruption, angiogenic imbalance, fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or intrauterine fetal death).

DIAGNOSI DIFFERENZIALE

- flussimetria Doppler utero-placentare (FGR)
- sFlt1/PlGF

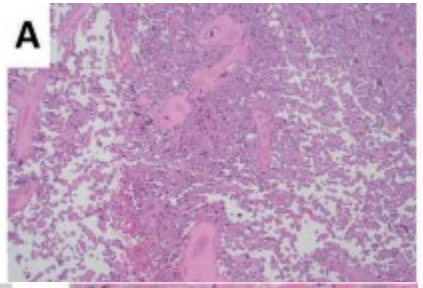
Piccoli GB et al. Hypertension in CKD Pregnancy: a Question of Cause and Effect (Cause or Effect? This Is the Question). Curr Hypertens Rep. 2016.
Magee LA et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens. 2022

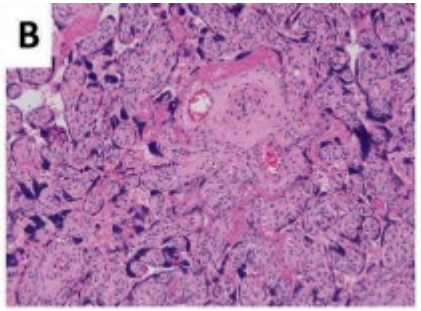
Rapporto acido urico/creatinina: marker di preeclampsia?

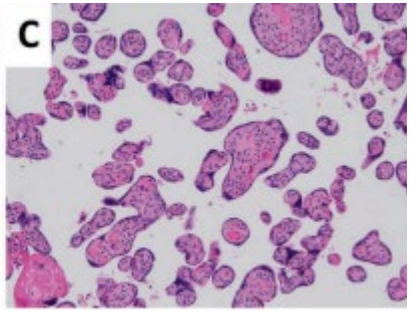


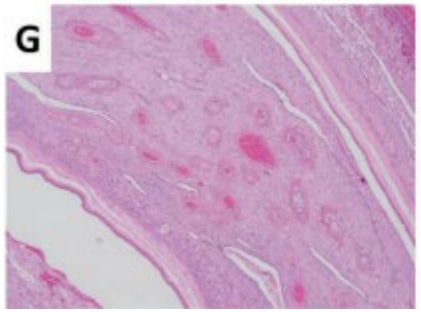
Piani F et al. HDP Bologna Study Group. Serum uric acid to creatinine ratio and risk of preeclampsia and adverse pregnancy outcomes. J Hypertens. 2023

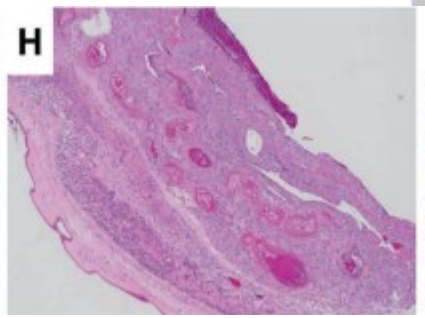
Placenta

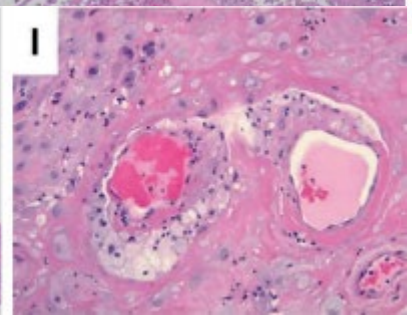












Diagnosi

Macro

Placenta singola, pervenuta intera, fissata.

Segmento di cordone ombelicale biancastro, della lunghezza di cm 42 (diametro cm 1 circa), ad inserzione paracentrale (distanza dal bordo del disco coriale: cm 3 circa), normospiralizzato (circa 3 giri /10 cm), con twist levogiro; presenti due falsi nodi posti a cm 8 e cm 17 dall'inserzione sul disco.

Membrane normoinserite, opache, complete, lacerate, ispessite, con punto di rottura non precisabile.

Disco coriale ovalare, delle dimensioni di cm 16x12 (spessore cm 2,5 - cm 1 circa) e del peso di g 308 circa. Versante fetale lucente; vasi coriali a distribuzione magistrale. Versante materno di colore normale, con cotiledoni integri, a profili regolari. Al taglio del disco, si evidenzia lesione biancastra retroplacentare del diametro massimo di cm 1.

Peso placentare <10° percentile

Micro

Cordone ombelicale a tre vasi.

Membrane con ipertrofia murale delle arterie della decidua parietale ed associata aterosi.

Villi coriali del terzo trimestre con aspetti di accelerata maturazione.

Ectasia dei vasi corion-allantoidei.

La lesione di cui al referto macro corrisponde a deposito perivilloso di fibrina, localizzato.

Decidua sede di arterie muscolarizzate (arteropatia deciduale gravidica) con associata aterosi; adesi fascetti di miometrio.

Maternal vascular
- Maldevelopment
- Malperfusion

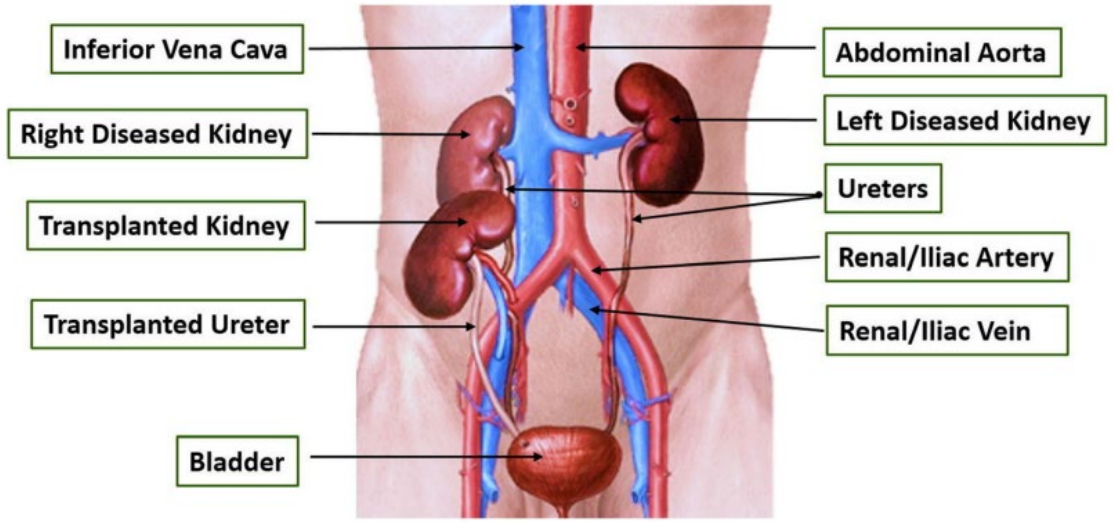
Redline RW et al. Four major patterns of placental injury: a stepwise guide for understanding and implementing the 2016 Amsterdam consensus. Mod Pathol. 2021
Redline RW et al. Placental pathology is necessary to understand common pregnancy complications and achieve an improved taxonomy of obstetrical disease. Am J Obstet Gynecol. 2023

…Taglio cesareo a 32+ 6 wks

Prevalenza di lesioni del graft durante taglio cesareo <1%

Non ci sono raccomandazioni specifiche su come prevenire lesioni del graft:

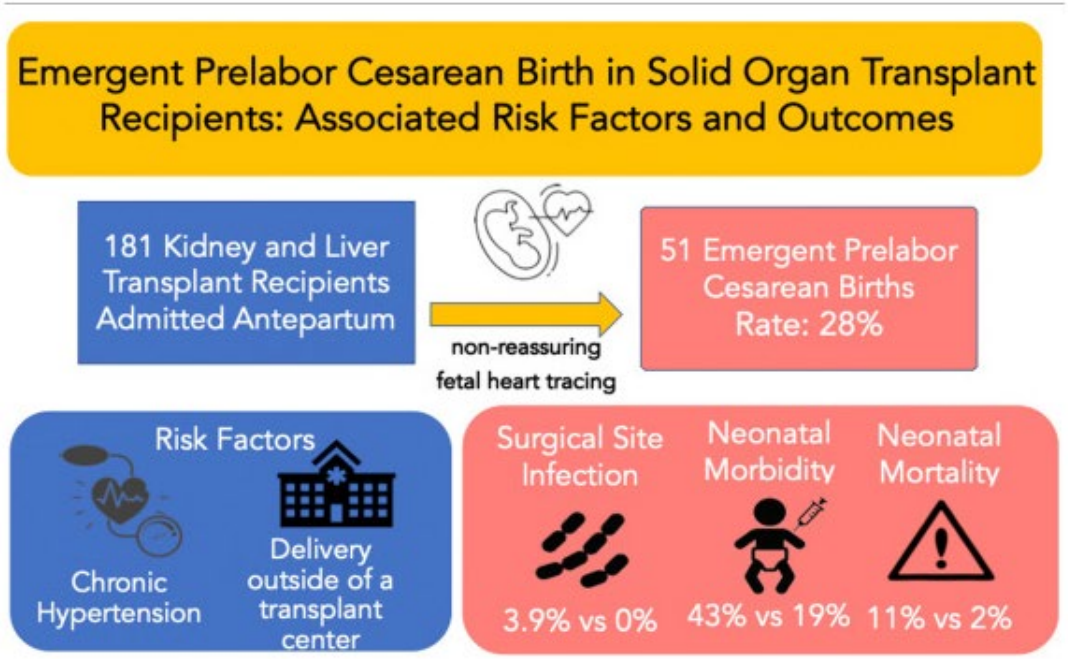
- Attenta dissezione dei tessuti (aderenze del graft con fascia e/o peritoneo)
- Non controindicazioni a incisione cutanea trasversale



- **Team multidisciplinare (chirurgo ostetrico esperto e disponibilità team chirurgico specializzato in trapianti)**

- Disponibilità di emoderivati
- Localizzazione ecografica del rene e studio dell'anatomia

Gordon CE Shearing-force injury of a kidney transplant graft during cesarean section: a case report and review of the literature. BMC Nephrol. 2019
Yin O et al. Mode of Obstetric Delivery in Kidney and Liver Transplant Recipients and Associated Maternal, Neonatal, and Graft Morbidity During 5 Decades of Clinical Practice. JAMA Netw Open. 2021



- Studio retrospettivo di coorte di tutte le riceventi di trapianto di rene e fegato a >20 settimane di gestazione

- Transplant Pregnancy Registry International 1976 - 2019.

- L'indicazione più frequente taglio cesareo: CTG non rassicurante.
- Taglio cesareo urgente fuori travaglio associato a :
  - prematurità
  - morbilità neonatale

- Fattori di rischio:
  - ipertensione preesistente
  - Espletamento del parto al di fuori di un centro trapianti.

Chung K et al. Emergent prelabor cesarean delivery in solid organ transplant recipients: associated risk factors and outcomes. Am J Obstet Gynecol MFM. 2023

Trapianto di rene e fertilità

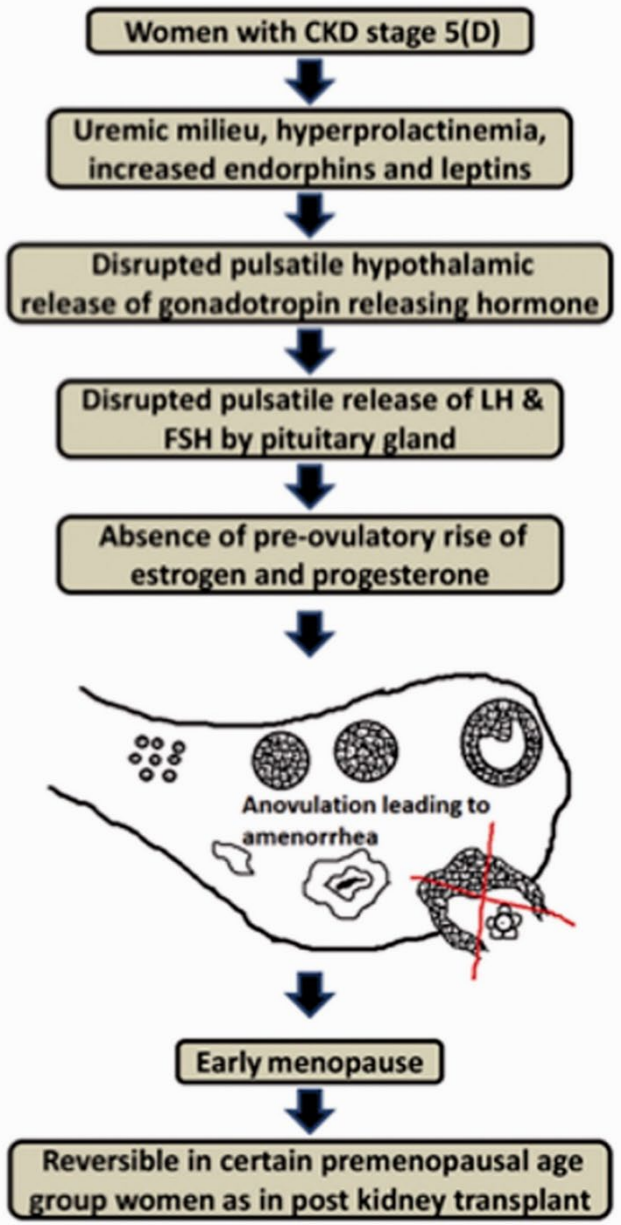


Table 4. Live-born rates in on dialysis and after kidney transplantation, as compared with the overall Italian population

	Live births in the overall dialysis and transplant populations	Patient-years of observation age 20–45 females	Live-birth rate age 20–45 per 1000 subjects	Baseline employed data and assumptions followed
Dialysis patients	24	22 000–35 000	0.7–1.1	24 Births observed the whole population. Inference for M:F = 60:40. Age 20–45 = 10% of the overall population. Prevalent dialysis patients: range of the estimation 36 000–50 000. Stable prevalence in 2000–12 in the age group 20–45.
Kidney transplant patients	183	22 000–33 000	5.5–8.3	110 Live births observed in mothers with a kidney graft, with data available from the transplant centres covering ~60% of the Italian population. Inference for M:F = 60:40. Age 20–45 = 30% of the overall population. Prevalent grafted patients: range of the estimation: 18 000–21 000. Stable prevalence in 2000–12 in the age group 20–45.
Italian population	–	–	72.5	Italy ~60 million inhabitants stable birth rates in the period 2000–12. Overall population live-birth rate: 9.02; inference for M:F = 50:50; age 20–45 = 25% of the overall population; due to the very low birth rate in the ages 15–19, the rates were referred as due only to the 20–45 years age group, in females only.

Gravidanza in CKD:

- Stadio 1-2 3% delle donne in età fertile
- Stadio 3-5 1:150-1:750 donne in età fertile

Piccoli GB et al. Italian Study Group "Kidney and Pregnancy". The children of dialysis: live-born babies from on-dialysis mothers in Italy--an epidemiological perspective comparing dialysis, kidney transplantation and the overall population. Nephrol Dial Transplant. 2014

Reynolds ML, Herrera CA. Chronic Kidney Disease and Pregnancy. Adv Chronic Kidney Dis. 2020.

Gravidanza dopo trapianto di rene: tante domande e poche risposte

What is a successful pregnancy for a woman with significant kidney disease?
Is it ultimately achieving a “baby in arms” regardless of the journey,
or is it a minimally complicated pregnancy with a well-grown, near-term baby?

- Un tempo la gravidanza era «non sconsigliata» solo quando la funzione del trapianto era normale, la proteinuria assente e la paziente era normotesa, senza rischio di rigetto.
- Attualmente con l’accettazione di donatori e riceventi con criteri di "alto rischio", le gravidanze "ideali" dopo il trapianto di rene stanno diventando un'eccezione.
- Approccio centrato sul paziente: le donne informate e responsabilizzate accettano il rischio di gravidanza a favore del raggiungimento dei loro obiettivi personali di maternità.
- Counseling preconcezionale

Jesudason S, Piccoli GB. Pregnancy outcomes after kidney transplantation: the challenges of success. Kidney Int. 2022

Grazie per l’attenzione