

Dialysis on Pregnancy

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Contributor: Valentina Del Negro

Pregnancy rates in women on dialysis have increased in the last decades, thus making it a topic of growing interest. The rarity of this event is predominantly due to fertility problems and to the high rates of pregnancy failure including stillbirth, fetal, and neonatal deaths.

dialysis in pregnancy

end stage renal disease

hemodialysis

peritoneal dialysis

intensive dialysis regimen

preeclampsia

1. Introduction

Pregnancy in women on dialysis is not common, but is becoming increasingly topical. The rarity of this event is predominantly due to fertility problems and to the high rates of pregnancy failure including stillbirth, fetal and neonatal deaths [1]. Moreover, the majority of women with renal insufficiency pursue pregnancy at more advanced ages and can be afflicted by underlying diseases [2]. Therefore, these women represent a population of high risk-patient, with increased rates of adverse pregnancy outcomes, including abortion, preeclampsia, preterm delivery, fetal growth restriction, low birth weight and higher frequency of neonatal intensive care unit admissions [3]. Women with advanced stages of chronic kidney disease (CKD) may also have further deterioration of kidney function after pregnancy [1].

Since the first successful case of pregnancy on hemodialysis described in 1971 by Confortini et al. [4], the incidence of pregnancies complicated by CKD is becoming more and more frequent and increasingly being encountered in obstetrical practice. It is estimated that CKD affects about 3% of pregnant women in high-income countries, and its prevalence will further grow, due to advanced maternal age and obesity [5]. Literature evidence suggests a six-fold increase of the number of dialysis pregnancies from the years 2000–2008 compared to the years 2008–2014 [6], even though the probability of becoming pregnant for this group of women is about 1:100 if compared to the general population of the same age [7]. This increment of cases could be related to improved medical care, in particular intensive dialysis regimens, better blood pressure control, adequate maternal nutrition with supplementation of iron, vitamins, folic acid, and erythropoietin, and multidisciplinary monitoring [8]. Despite renal transplantation for women with end stage renal disease (ESRD) offers better perspectives to reach improved pregnancy outcomes [7], we should highlight that, even if complicated to manage, pregnancy on dialysis is achievable, although it is still high-risk.

Even though the topic of dialysis on pregnancy is becoming increasingly frequent, there is still not a clear consensus in literature on how to treat patients on dialysis in pregnancy and no precise guidelines. The aim of this narrative review is to give to the reader an exhaustive and updated overview on all aspects regarding this important topic, from conception to birth, both including obstetrical and nephrological insights, in order to guide their work from pre-pregnancy counseling to pregnancy management and delivery.

All indications provided are resumed in Table 1.

Table 1. How to manage pregnant women on dialysis.

	Women with end stage renal disease (ESRD) frequently experience reduced fertility.
Fertility	Conceiving before dialysis, even if dialysis is commenced and continued during pregnancy, is related to highest live birth rates compared to dialysis already established at conception (91% versus 63%; $p = 0.03$).
	The safest method to confirm pregnancy and calculate gestational age is ultrasound assessment.
Pregnancy Diagnosis	Non-invasive screening should not be recommended because beta hCG and maternal serum PAPP-A levels are increased in women on dialysis due to decreased renal clearance.
Dialysis Technique: Peritoneal Dialysis and Hemodialysis	Dialysis treatment should begin earlier in pregnant patients. In literature, no differences regarding gestational outcomes between hemodialysis (HD) and peritoneal dialysis (PD) are reported. Data on PD are limited, probably because of the lower diffusion in the general population of this technique compared to HD and because pregnancy rates are lower in this group of patients. There is no clear consensus in literature on the most appropriate dialysis technique (HD or PD) to start in case of acute renal injury presenting for the first time during gestation. In pregnant women already on dialysis there is no indication to change dialysis technique, treatment regimens should be intensified to achieve better gestational outcomes.

Intensive dialysis regimens are associated with positive correlation with pregnancy outcomes.

Nutrition

Literature data recommend energy requirements related to pre-gestational weight, adding pregnancy energy needs and weight gain during the trimesters. It is also recommended to control interdialytic weight gain.

Women should receive supplemental oral iron and folic acid, electrolytes, and vitamins.

Maternal Outcomes

Hypertension is very common and preeclampsia (PE) occurs in up to 40% of pregnant women with CKD. Superimposed preeclampsia is difficult to diagnose in patients with underlying kidney disease.

Other several adverse outcomes are miscarriage, anemia, infection, premature rupture of membranes, eclampsia, increased hemorrhagic risk, and maternal death.

Fetal Outcomes

Preterm delivery and intrauterine fetal growth restriction are common in patients with ESRD on dialysis and preterm birth in these patients is often medically indicated.

The incidence of SGA neonates in ESRD patients is estimated at about 50%. SGA on HD is lower as compared to PD.

Polyhydramnios can occur in about 30–70% of the pregnancies.

Pre-Pregnancy Counselling and Contraception

Pregnancy should be postponed in the case of active immunologic diseases and the exposure to teratogenic drugs should be avoided. Women also should be assisted in managing correctly other comorbidities, like diabetes and systemic lupus erythematosus.

Clinicians should advise women about the possibility of contraception. Progestogen only methods are safer because of the reduced side effects in patients at a high risk of thromboembolism and hypertension.

2. Fertility

First of all, it is well known that women with ESRD frequently experience reduced fertility. It has been hypothesized that the decline of glomerular filtration rate (GFR) and uremia leads to dysregulation of the hypothalamic-pituitary-ovarian axis [9]. In fact, constantly increased luteinizing hormone (LH) levels lead to loss of cyclical hormones variability and absence of mid-cycle LH surge, with suppression of ovulation [10]. Moreover, impaired renal clearance of prolactin and resulting high circulating levels of this hormone contribute to ovulation failure [11]. Sexual dysfunction is also usual in these patients manifesting as reduced libido, dyspareunia, altered body image, and depression [12].

Some aspects of dialysis treatment in ESRD seem to be crucial to achieve a successful pregnancy. Jesudason et al. found that conceiving before dialysis, even if dialysis is commenced and continued during pregnancy, is related to highest live birth rates compared to dialysis already established at conception (91% versus 63%; $p = 0.03$) [13]. This is probably due to the residual renal function in patients who conceive before dialysis, which, on the contrary, often declines in women already subjected to dialysis [14][15].

3. Pregnancy Diagnosis and Management of Early Gestation

Because of irregular menstrual periods, pregnancy is not easy to detect in the early phases in women with ESRD and the diagnosis is often delayed at about 16.5 weeks of gestation [15]. BetahCG levels are unreliable, since they are always increased in dialysis patients, even in non-pregnant ones. Therefore, the safest method to confirm pregnancy and calculate gestational age is ultrasound assessment [16]. Because of decreased renal clearance, besides betahCG, also maternal serum PAPP-A levels are increased in women on dialysis, therefore non-invasive screening is not appropriate and should be not recommended. Moreover, the performance of cell free DNA testing in this type of population is not well known [17]. During prenatal counselling, the health-care provider should advise these women that invasive prenatal screening is the only reliable method to detect fetal genetic abnormalities. However, rates of fetal malformations in mothers with renal failure seem comparable to those seen in the general population (approximately 2%), except for diabetic nephropathy, hereditary diseases and use of teratogenic drugs [6].

4. Dialysis Technique: Peritoneal Dialysis and Hemodialysis

Dialysis during gestation may be necessary for various causes. There is the possibility of a pre-existent renal pathology worsening during pregnancy and requiring dialysis, or the condition of women previously affected by ESRD becoming pregnant, but acute renal injury could also present for the first time during gestation [18]. In literature, no differences regarding maternal and fetal outcomes between hemodialysis (HD) and peritoneal dialysis (PD) are reported [19], and none of the techniques seems to influence negatively the infant survival rate [20]. Nevertheless, it is necessary to specify that literature data on PD are limited, probably because of the lower diffusion in the general population of this technique compared to HD and because pregnancy rates are lower in this

group of patients. The mechanism supposed to be involved is that intraperitoneal hypertonic solutions may be associated with inflammatory effects on the fallopian tube and the uterus, interfering with embryo implantation [3].

In case of acute or rapidly progressive chronic renal disease, the most important management choice to do is when to start the treatment. There are no specific values beyond which it is mandatory to start dialysis, and validated methods for the assessment of residual renal function in pregnancy do not exist [3]. Nevertheless, it is clear that the dialysis treatment should begin earlier in pregnant patients and generally should be considered for values of serum creatinine of 3.5–5.0 mg/dL and for GFR < 20 mL/min [21][22]. Clinicians may also consider commencement of dialysis when urea is >17 mmol/L [23], because fetotoxicity of urea is more important than any maternal indication to begin dialysis [3].

There is no clear consensus in literature on the most appropriate dialysis technique (HD or PD) to start in case of acute renal injury presenting for the first time during gestation.

Data reported in literature on HD are much richer than those on PD because of the higher number of patients on HD and the good pregnancy outcomes reported. Nevertheless, there is only one author, Vazquez, in 2010 clearly reporting HD as the first choice in pregnant women or postpartum period complicated by acute renal insufficiency or in case of worsening of renal function at the time of conception [24]. However, it is reasonable to think that HD, being the most frequently-used technique, is therefore the most suitable one in case of acute renal injury occurring for the first time in pregnancy, especially considering the acute technical difficulties associated with peritoneal dialysis treatment (positioning and maturation of the Tenckhoff catheter).

In pregnant women already on dialysis there is no indication to change dialysis technique, as suggested by the Italian Study Group on Kidney and Pregnancy in 2015 [16]. The recommended strategy is that treatment regimens should be intensified to achieve better gestational outcomes, so to reduce interdialytic weight gain and fetal exposure to harmful substances [18].

Intensive dialysis regimens are associated with higher conception rates and have a positive correlation with pregnancy outcomes, including gestational age and birth weight, having an influence on placental development that is crucial for fetal well-being [25]. Retrospective data demonstrate that more intensive dialysis schedule, increasing the number of hours from <20 to >36 h per week, is associated with regularization of menstrual cycles, better neonatal outcomes and live birth rate growth from 48 to 85%, with a positive dose response ratio [25].

There are several advantages of intensive HD in pregnancy. Intensive HD facilitates excess fluid removal so there is less variation in intra-dialytic blood pressure [25], which allows better control of blood pressure, reducing the use of antihypertensive agents and diuretics [24][25] compared to standard dialysis (≤20 h/week), and also increases clearance of uremic toxins that improves pregnancy outcomes [25].

High biocompatibility dialyzers are recommended [24] because a lower surface area avoids excessive fluid loss with less episodes of hypotension and changes in osmolality [26].

Although there are several risks of pregnancy-related complications, intensive PD regimens can be used and do not induce metabolic changes also allowing a gradual fluid control, so controlling blood pressure [15]. However, PD could negatively-influence maternal nutrition status and could require lower dialysate volumes because of overdistension of the uterus in the late trimester of pregnancy [22].

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