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Risk Factors for Adverse Fetal Outcome in Hemodialysis Pregnant Women

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Introduction: Pregnancy in women on dialysis is associated with a higher risk of adverse events, and the best care for this population remains to be established.

Methods: In this series, we aimed to identify factors associated with the risk of adverse fetal outcomes among 93 pregnancies in women on hemodialysis. Dialysis dose was initially assigned according to the presence of residual diuresis, body weight, and years on dialysis. Subsequent adjustments on dialysis dose were performed according to several parameters.

Results: The overall successful delivery rate was 89.2%, with a dialysis regimen of 2.6 ± 0.7 h/d, 15.4 ± 4.0 h/wk, and mean weekly standard urea Kt/V of 3.3 ± 0.6. In the logistic models, preeclampsia, lupus, primigravida, and average midweek blood urea nitrogen (BUN) level were positively related to the risk of a composite outcome of perinatal death or extreme prematurity, whereas polyhydramnios was inversely related to it. In multivariable linear regression, preeclampsia, polyhydramnios, primigravida, average midweek BUN, and residual diuresis remained significantly and independently related to fetal weight, which is a surrogate marker of fetal outcome. An average midweek BUN of 35 mg/dl was the best value for discriminating the composite outcome, and BUN ≥35 mg/dl was associated with a significant difference in a Kaplan-Meier curve ($P = 0.01$).

Conclusion: Our results showed that a good fetal outcome could be reached and that preeclampsia, lupus, primigravida, residual diuresis, polyhydramnios, and hemodialysis dose were important variables associated with this outcome. In addition, we suggested that a midweek BUN <35 mg/dl might be used as a target for adjusting dialysis dose until hard data were generated.

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Although still uncommon, dialysis during gestation is becoming more frequent.[1–4] In the only study that evaluated trends along time, the pregnancy rate in women on dialysis has risen from 0.54 to 3.3 pregnancies per 1000 patients-years in the last 3 decades.[5] Although a substantial improvement in pregnancy outcome has occurred,[6] pregnancy in patients with chronic kidney disease (CKD) who are on dialysis still carries a significant risk of adverse events.[7,8]

In this sense, nephrologists are faced with the difficult task of dealing with high-risk pregnancy, which carries increased odds of adverse events for both the mother and fetus. Several questions arise in the attempt to establish the best care for pregnant women on dialysis, and issues such as the best moment to start renal replacement therapy, dialysis dose, and schemes are a matter of intense debate. Comparisons are hard to make due to differences in patient profiles, dialysis modality, dialysis schemes, obstetric definitions, and obstetric protocols, as previously discussed.[6] Protocols vary widely, and there is clearly a need for standardization and establishment of guidelines that particularly focus on improvement of fetal outcomes. Although there is some evidence that suggests that a more intensive dialysis dose is related to a better fetal outcome, the optimal dialysis regimen and dose remain to be established.[9–13]

In the present study, we reported our experience with 93 pregnancies in women who underwent hemodialysis (HD) from 2000 to 2017, which is currently the largest single-center series. In the analysis, we aimed to identify baseline risk factors for pregnancy outcomes and to evaluate the association between several dialysis parameters and the risk of adverse events.

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METHODS

Study Design and Population

This retrospective cohort study consisted of 93 pregnancies in women who underwent HD at Hospital das Clínicas, Faculty of Medicine, University of Sao Paulo, Brazil, from January 2000 to January 2017. During that period, 100 pregnant women were referred to our dialysis center. Seven patients were not included in this case series: 1 patient with acute renal failure, 2 patients who had HD for <15 days before delivery, 1 patient with multiple fetal losses before developing renal failure, 2 patients with a severe lupus flare that required intensive immunosuppression when the referral to the nephrological team was made, and 1 patient with osteogenesis imperfecta, a disease associated with poor fetal prognosis,[14] which left 93 pregnancies for the analysis. For patients with >1 pregnancy (n = 4), all pregnancies were included. The study was approved by the Ethics Committee and was conducted in accordance with the Declaration of Helsinki. In a previous publication,[13] we reported outcomes in 52 pregnancies that occurred from 1988 to 2008. In the present analysis, we excluded 18 pregnancies that occurred from 1988 to 1999 that were included in the previous publication because by that time a different dialysis regimen was prescribed (time-fixed, 3-hour sessions, 4−6 times weekly). Erythropoietin was not provided for 9 patients, and many advances in obstetric surveillance and neonatal care were not available. Thus, the present report included 34 pregnancies that occurred from 2000 to 2008 reported in the 2010 publication and 59 new pregnancies that occurred after 2008.

Dialysis Protocol

Pregnant women who underwent HD received a high-flux, high-efficiency, 6 times/week HD scheme (dialyzer 1.8 m^2, high-flux polysulfone, Kuf 55 ml/h per mm Hg, blood flow 350 ml/min, and dialysate flow 800 ml/min). The dialysis regimen was individualized. Patients with diuresis of >1000 ml/d, <1 year on HD therapy, or with a body weight <70 kg were initially assigned to 1.5- to 2 hour sessions, whereas patients with diuresis of <1000 ml/d, >1 year on HD therapy, or body weight >70 kg were assigned to a 2- to 3-hour session. Throughout pregnancy, adjustment of dialysis dose followed 2 different protocols. In protocol 1, from January 2000 to December 2008, the dialysis regimen was adjusted according to the laboratory, ultrasonographic, and clinical parameters. Severe hypertension, anorexia, frequent nausea, excessive weight gain, and persistent polyhydramnios, were all treated with a 30-minute increase in HD time. In protocol 2, from January 2009 to January 2017, in accordance with our findings that an average midweek blood urea nitrogen (BUN) <35 mg/dl was associated with a better fetal outcome,[13] in addition to the parameters from protocol 1, the dialysis dose was also increased as needed to keep the midweek BUN at <35 mg/dl. For those who were not on dialysis, this treatment was started when an ascending creatinine reached 3.5 to 4.0 mg/dl. However, most of the patients arrived as late referrals, with creatinine values far above this value (initial creatinine range: 3.3−9.7 mg/dl, and a median creatinine clearance of 11.7 ml/min with an interquartile range [IQR] of 7.6−15 ml/min). Recombinant human erythropoietin dose (median dose: 24,000 IU/wk; range: 4000−48,000 IU/wk) was adjusted to maintain maternal hematocrit at 30% in both protocols.

Several dialysis parameters were measured, including average BUN (mean values for midweek predialysis BUN were collected Wednesdays or Thursdays), peripartum BUN, and creatinine. Single-pool Kt/V was determined using a 2-point urea model based on the intradialytic decrease in the blood urea level, intradialytic weight loss, and session length.[15] Kt/V reported here was the mean of several values collected throughout the pregnancy; number of measurements 3.7 ± 2.3). Weekly standard urea Kt/V (stdKt/V)[16] was estimated for all patients using the Leypoldt proposed formula.[17] Hours on dialysis per week were defined as the longer scheme prescribed during treatment. Diuresis in milliliters per day and residual creatinine clearance were measured in a 24-hour urine collection (at the initiation of renal replacement therapy for those starting dialysis after conception or soon after pregnancy diagnosis for patients already on dialysis), and renal Kt/V was ascertained. Creatinine clearance and renal Kt/V were not ascertained in 20 patients because these measurements were not regularly performed in the beginning of our series. In 3 patients with diuresis of <200 ml/d, renal Kt/V was considered zero.

Obstetric Protocol

All participants followed a high-risk antenatal care protocol, defined as frequent prenatal and fetal monitoring, a low threshold for hospitalization, and a well-timed delivery. Low-dose aspirin and calcium supplementation were prescribed before gestational week 12, if not otherwise contraindicated, for preeclampsia prevention. Prenatal office visits were made every month up to 20 weeks and twice a month or weekly thereafter. Patients were actively monitored for signs and symptoms of preeclampsia. Both clinical (severe headache, visual change, and epigastric and right hypochondrium pain) and laboratory parameters (low platelet counts, increased liver enzymes, hemolysis, and increased proteinuria) were checked. Fetal