



## ORIGINAL ARTICLE

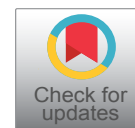
## Increased Hemodialysis Sessions during Pregnancy Improve Fetal Development and Reduce Mortality: Literature Review

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### Abstract

Renal failure is a chronic disease of complex treatment and has a great impact on people's quality of life. Pregnancy in women on renal replacement therapy is considered high risk, requiring specific care to promote adequate treatment and improvement in maternal and fetal outcomes. This study consists in evidencing the effects of the increase of hemodialysis sessions on the health of pregnant women with Chronic Renal Insufficiency. The profile is based on women between 18 and 44 years of childbearing age. To this end, it seeks to identify the profile of women who become pregnant on dialysis treatment and outcomes. This is an integrative review, with selection of articles from the Virtual Health Library and the PUBMED from the last five years on the subject. The results show that increasing from four to six weekly hemodialysis sessions was related to decreased maternal-fetal mortality risks, and increasing gestational length from 31 to 34 weeks reduced rates of preterm births. The studies reviewed provide evidence of the benefit of increased hemodialysis sessions in dialysis pregnant women, reducing complications and improving the quality of life of the pregnant woman and the child.

### Keywords

Hemodialysis, Pregnancy on Hemodialysis, Hemodialysis sessions

### Introduction

Chronic Renal Failure (CKD) affects about 195 million women worldwide [1], however, pharmacological advancement and hemodialysis sessions in recent decades have demonstrated significant improvements in quality of life, well-being, and the outlook for life in women with chronic renal failure [2].

Renal replacement therapy is a treatment that contributes to the improvement of the patient's clinical condition and with it the quality of life. In recent years, there has been an increase in pregnancy rates among dialysis patients due to a combination of several factors, such as increased maternal age and the limited availability of organs for transplantation [3].

Women with CKD can present alterations in physiological and emotional aspects as a result of the disease, such as hormonal functions, causing: amenorrhea; anovulatory cycle; sexual dysfunction; decreased libido and reduced fertility [4].

Pregnant women on dialysis treatment are considered high risk, requiring clinical management by a multidisciplinary team during prenatal care due to renal overload caused by pregnancy [5,6]. Thus, this pregnant woman should undergo intensive hemodialysis (HD) of 20 hours per week at the hospital level to perform hydroelectrolytic and weight control, urea levels < 30-50 mg/dl and minimal heparinization required [5].

Regarding the risks inherent to pregnancy in women with CKD, a higher rate of maternal and fetal morbidity and mortality with preterm birth is identified, including rates of low birth weight, also having aggravating factors such as anemia, hypertension, diabetes, HELLP syndrome [6]. Thus, pregnant women on dialysis represent a challenge for the care team, which requires a multidisciplinary management, as well as the adaptation

of the substitutive renal treatment scheme to ensure an improvement in their well-being and safety [6].

Intensification of dialysis treatment is part of best clinical practice, improving pregnancy outcomes. HD frequency is intended to increase the treatment time and frequency of dialysis sessions, maintaining low levels of uremic toxin and ensuring hemodynamic stability, avoiding effective hypovolemia, intradialytic hypotension and large osmotic and electrolyte fluctuations [7].

Therefore, this study is an integrative literature review, which aims to highlight the effects of increased hemodialysis sessions on the health of pregnant women with CKD, seeking to identify the profile of women who become pregnant on dialysis treatment and outcomes.

## Methodology

This study is an integrative literature review on the theme related to the scientific knowledge concerning pregnant women on hemodialysis. The Integrative Literature Review uses the evidence found within the literature itself with the intent of scientific knowledge, with the effect of quality and good cost-benefit seeking the evaluation of the results.

Thus, the integrative methodology is divided into 6 parts [8]: in the first part, the researcher must choose the central question of his work, with the intention of being answered throughout the work. To do so, the guiding question was formulated using the PICO method (P - population; I - interest; CO - context), thus, in this work, the "P" is related to the pregnant woman, the "I" is related to the increase of hemodialysis sessions and the "CO" is related to chronic renal failure; the following question was raised: "What are the effects of the increase of hemodialysis sessions on the health of pregnant women with chronic renal failure?".

In the second part, a bibliographic research was carried out, using two digital databases such as the Virtual Health Library (VHL) and the National Library of Medicine (PUBMED). The following keywords were used: Hemodialysis pregnancy, hemodialysis pregnancy, and chronic kidney failure.

The selection factors used to select the sample were as follows: studies from the last 10 years, containing a positive methodology, taking into consideration the areas of interest of the theme, being complete texts, available online. This period was chosen because of its increasing frequency within healthcare and the fact that the use of more or longer hemodialysis sessions has intensified in recent years.

An initial sample was obtained from a literature search conducted in December 2021. Over the following months, exploratory readings were performed of the titles and abstract of the articles, followed by floating reading to check if they were suitable for the proposed

topic. Next, selective literature, that is, a more in-depth reading of the full text of the article, was performed. Studies not related to the research topic were excluded from this literature. The inclusion criteria for the selection of articles were: articles published in Portuguese and English, articles available in full, describing relevant themes for the comprehensive review, and articles published indexed in the databases in the last decade. Then, after determining the final sample, an analytical reading was performed in order to prioritize and summarize the information contained in the selected articles in response to the research objectives.

For this, a total of 62 articles were selected from the Virtual Health Library (VHL) database and 73 articles from the National Library of Medicine (PUBMED). However, 131 articles were excluded by the criteria of title, abstract, methodology, and duplicates, totaling 4 articles selected for this research.

Regarding the inclusion criteria, articles published in Portuguese and English, published in the last five years (2017-2022) participated in this research. To this end, we chose to exclude articles that did not address the theme studied, as well as monographs, dissertations, theses, manuals and ordinances.

In the third stage, which aims at the organization that collects data, we used proper forms for data collection to record the information considered most important for the objectives of this study. Therefore, the final sample was organized in descending order of year of publication.

The fourth step is the critical analysis of the selected studies, that is, the analysis and synthesis of data extracted from the articles in a descriptive way, which enables the observation, enumeration, description, and classification of data in order to gather the knowledge generated about the theme explored in the review.

The fifth stage aims to show the main results of the articles chosen for the research. It integrates the reduction, exposition and comparison, data verification, and the identification of gaps in suggestions for future research.

Finally, the sixth stage is characterized by the presentation of the integrative review and the synthesis of knowledge, aiming to encourage the reader to critically evaluate the results [8]. So, the important and detailed information is presented without omitting any related evidence.

## Results and Discussion

Table 1 below lists the data obtained by researching the most pertinent articles that are related to this study. To this end, the information considered most important was registered, organized in descending order of year of publication and alphabetical order of the author's last name, respectively. The table contains data such

**Table 1:** Data obtained through the survey and its characterizations.

Title, Author and Year	Objective	Methodology	Results
Pregnancy outcomes in hemodialysis patients in France.  Normand, et al., 2018 [9].	To describe the maternal characteristics and risk factors associated with maternal and fetal maternal and fetal outcomes.	Descriptive, retrospective, multicenter study. Pregnant women on hemodialysis during the period 1985 to 2015 in France were included.	It revealed that the benefit of increased hemodialysis sessions in pregnancy was confirmed through higher mean birth weight (2,400 g) and an increased fetal survival of 85%. The mean duration of dialysis per week was 18 ± 4.2 hours, while at least 20 hours of dialysis per week are associated with significantly improved fetal outcomes. Given the apprehended results, increased hemodialysis sessions during pregnancy contributed in 85% of women to fetal survival. This was more than 36 hours of hemodialysis per week compared to 48% of those with lower income who received 20 hours of dialysis.
Obstetric deliveries in US women with Chronic Renal Insufficiency: 2002-2015  Oliverio, et al., 2020 [6].	To describe long-term trends in obstetric deliveries among women with chronic kidney disease in the United States and to investigate the association of treatment modalities (hemodialysis, peritoneal dialysis, and transplantation) and other clinical characteristics with delivery outcomes, including premature delivery and cesarean section.	We conducted a retrospective cohort study of all female CKD patients between January 1, 2002 and September 30, 2015, using data from the United States Renal Data System (USRDS).	It showed a 71% increase in the birth rate among women of childbearing age on hemodialysis during the study period. It was found that although the average number of hemodialysis minutes prescribed increased slightly in the 9 months prior to delivery, only a minority of women received more than 1,200 minutes of hemodialysis per week in their outpatient hemodialysis units. In addition, birth rates increased from 2.1 to 3.6 per 1,000 patient-years and from 3.1 to 4.6 for women who received hemodialysis and those who received renal transplantation, respectively. And, the mean age at delivery increased from 29.1 years in 2002 to 31.9 years in 2015 during the study period. Among mothers, 81.8% preferred hemodialysis, 12% preferred peritoneal dialysis, 5.9% transplanted first, and the remaining 0.3% had an unknown first choice. Thus, those receiving peritoneal dialysis had lower chances of delivery, and older age was also associated with lower chances of delivery, with a 41% rate of premature delivery.  Black women on chronic kidney dialysis were more likely to have a premature birth than white women, and noted that 50.6% of transplant recipients gave birth by C-section.
Pregnancy in chronic hemodialysis: about 25 cases occurring in southern Tunisia.  Chaker, et al., 2020 [10].	To report the experience on the occurrence of pregnancy in dialysis patients and identify the factors involved in its success.	A retrospective study of 25 spontaneous pregnancies that occurred in 19 patients treated with periodic hemodialysis in southern Tunisia over a period of 34 years.	It was noted that with adequate support and especially increasing the number of dialysis sessions, maternal-fetal complications can be minimized.  Sixteen hours of dialysis per week was scheduled, which occurred in 7 cases and 20 hours per week, resulting in newborn survival and a mean gestational age of 34 weeks. Analysis shows that there is a significant correlation between increases in weekly dialysis time and gestational success rate (R = 0.59; p = 0.002).
Pregnancy and its outcomes in hemodialysis patients in Turkey.  Dheir, et al., 2021 [11].	Investigate the frequency of pregnancy and assess factors affecting live births in hemodialysis patients.	Female hemodialysis patients whose pregnancy was reported retrospectively between January 1, 2014 and December 31, 2019.	The results of pregnancy in female patients on hemodialysis, showed that increasing the number of hemodialysis sessions decreases fetal and maternal complications and increases live birth rates.  The miscarriage rate was 22.4% in the group of women who had more hemodialysis sessions, compared to those who had fewer hemodialysis sessions who had a 79.3% miscarriage rate. In a dialysis 5 times a week was correlated with better.

Source: Prepared by the author (2022).

as year, author, title, journal, type of study, and what it says about the subject.

The selected studies evidenced the benefits of increasing weekly hemodialysis sessions during

pregnancy. Since, the increase of dialysis in patients in gestational period has collaborated significantly to the occurrence of successful deliveries, increased fetal survival [9].

The data regarding the profile of this parturient brings that the women became pregnant with the age between 30 to 34 years, and the studies Normand, et al. [9] and Chaker, et al. [10] emphasize that these pregnancies were unplanned, not making use of contraceptive method, discovering the pregnancy from 7 to 14 weeks. The studies showed that most of the deliveries were cesarean sections, and there were cases of vaginal delivery, but in smaller numbers due to the gestational age of the mother. Based on these data, it is possible to consider that unplanned pregnancy brings concerns, considering that these patients could have performed family planning and prepared better for pregnancy.

Increased dialysis leads to fewer maternal complications, and this is associated with higher birth weight and gestational age at delivery. Thus, hemodialysis sessions in the gestational phase should be increased to six sessions per week, which leads to an increase in the live birth rate by 71.7%, decreasing maternal fetal complications, premature birth rates, and increasing the gestational age of the pregnant woman from 31 to 34 weeks, i.e., significantly improving the outcomes of a successful pregnancy [11].

According to the studies of Normand, et al. [9], the woman with renal insufficiency presents maternal and fetal risks in pregnancy and largely, the infants are born prematurely. However, Oliverio, et al. [6], demonstrated in his study that despite the gestational difficulties, in recent years, there are reports of successful pregnancies, improving and preventing prematurity one of the main aggravations of this disease.

However, it is known that becoming pregnant with kidney failure poses health risks to both the woman and the fetus. Patients face the risks of maternal and fetal morbidities, pre-eclampsia and fetal death, and more premature births compared to the general population [6]. These women face uncertainty about their own survival and disease progression. In view of the above, it is understood that dialectic women of childbearing age can become pregnant, but in contrast, they prove high rates of both maternal and fetal complications [9].

Oliverio, et al. [6], brings a study of patients enrolled in the United States Renal Data System (USRDS) from 2002 to 2015, where it was observed that the rate and delivery in HD women increased from 2.1 to 3.6 per 1,000 patient-years, with 75% of women having hemodialysis prescription equal to or less than 4 times a week and 25% receiving accuracy of 5 or more HD sessions per week in the 30 days before delivery. Thus, the intensification of hemodialysis seems to explain the increased delivery rate among women treated with HD in the United States.

There is an overall improvement in HD pregnancy outcomes, observing 100 pregnancies in 84 women

on HD out of 41 [9]. Chronic HD was initiated during pregnancy in 17.7% of patients, explaining a 19.8% prevalence of catheter and residual diuresis preserved in 50% of pregnancy. Seventy-six (89.4%) women were on daily dialysis during the third trimester (6 times per week), with plasma urea concentration decreasing throughout pregnancy with a mean urea concentration of  $17.0 \pm 6.6$  mmol/L at the end of the first trimester ( $n = 72$ ) compared to  $13.4 \pm 4.5$  mmol/L at the end of the third trimester ( $n = 62$ ;  $p < 0.01$ ). Cesarean section was necessary for 62% due to hypertension, leading to outcomes with fetal survival at 78%.

Chaker, et al. [10] in their study showed a population of 25 spontaneous pregnancies that occurred in 19 patients treated by hemodialysis in different hemodialysis centers in southern Tunisia, finding that the number of weekly hours of prescribed dialysis was 16 hours per week in 7 cases and 20 hours in 4 cases. The mean hemoglobin level was  $8 \pm 1.54$  g/dl [5.1 10.6 g/dl] with use of erythropoietin in 12 cases (48%), phosphate in 11 cases (44%), intravenous iron in 11 cases (44%) and transfusion in 6 cases (24%). The mean urea level is equal to  $22.19 \pm 4.29$  mmol/L [14.66 - 28 mmol/L]. The analysis showed a significant correlation between increased hours of dialysis per week and successful pregnancy, decreasing the risk for the mother-child binomial.

Dheir, et al. [11], shows that the rate of increasing the number of dialysis sessions of patients during pregnancy was 71.7%, with this a rate of 67.2% live birth, 22.4% miscarriage and 10.4% stillbirth was observed in the sample. Furthermore, of those whose HD sessions were not increased, 3.4% resulted in live births, 79.3% in abortion and 17.2% in stillbirths, thus showing the effectiveness of increasing the HD sections which considerably decreases fetal and maternal complications, increasing the live birth rate.

In the studies analyzed, most of the pregnant women had benefits with the weekly increase of the HD section, both for their quality of life and for the possibility of developing a pregnancy. The 4 studies show the benefits presented, being one of them the maternal age that in the literature shows 30 weeks, in the studies they show a variation of 31 to 34 weeks, becoming an important data because, the more advanced, the better the chances of delivery and of possible vaginal delivery, decreasing the risks of a supposed cesarean section.

Dheir, et al [11], and Chaker, et al. [10], stated that live births had an improvement in birth weight gain of 1,750 to 2,045, raising the average birth weight bringing health to the fetus, helping intrauterine growth and development. The studies pointed out the increase in the live birth rate and decrease in fetal complications, improving the increase in obstetric deliveries by 50%.

These data show the need for a qualified nephrologist-

obstetric team so that the risk-benefit balance can transform a chronic renal woman's chance of becoming pregnant without further complications.

Thus, research proves that the increased frequency of hemodialysis is a beneficial practice for the reduction of maternal complications and improvement in quality of life, especially in pregnant women with intensive HD. With this practice, there was an increase in gestational age, decreased maternal-fetal risk, improved live birth weight, and increased fetal survival.

Normand, et al. [9], highlights that intensive dialysis of 36 h weekly improves fetal survival by 85%, and those performing 20 h weekly by 48%. While Chaker, et al. [10], evidences that the frequency of HD should be increased to 4 sections and then to 6 sessions per week from the fifth month, for metabolic control and the volemia and reduce urea levels, to thus have the results of improvement in pregnancy.

However, Dheir, et al. [11], reinforces that to maintain a successful pregnancy process, it should aim to reduce the exposure of dialysis patients to uremia during the week. Increasing the number of weekly HD sessions is essential in this regard, in addition to controlling weekly dry weight and ensuring adequate daily maternal-fetal calories.

In short, hemodialysis, through the present study, proved to be efficient because it is a beneficial practice for the reduction of problems caused by CKD, improving the quality of life, especially in pregnant women with CKD. Being observed that there is a shortage of recent clinical trials in relation to pregnancy in chronic renal disease patients on hemodialysis, which became a limitation for the study due to the small sample and also the methodological characterization of studies on family planning, which makes it susceptible to incomplete information, interfering directly in the dissemination of information that portrays the pregnant woman's profile in a real way.

## Conclusions

Dialysis treatment for pregnant women with CKD promotes a better quality of life for women, besides the improvement of maternal survival indicators. The challenge still thrives due to the diagnosed and inherent risks of this disease, according to studies.

With the increase of dialysis sessions progressively from four sessions to six weekly sessions, there is evidence of a decrease in the risks of death, both for the woman and the fetus. Though, this theme is still little discussed among professionals, and further studies on this topic may help to disseminate this information and improve the quality of life of pregnant women on hemodialysis.

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