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Case Report

The conception in hemodialysis: medical prognosis and experience of the gynecology-obstetrics department of Oujda on two cases

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ABSTRACT

Pregnancy in patients undergoing hemodialysis is a rare occurrence, particularly in Africa where therapeutic resources are limited, and is associated with high maternal-fetal risks. However, the incidence of pregnancies in such patients has increased over the past two decades, with notable improvements in prognosis and fetal survival, reaching 68.4% in some studies. This report describes two cases of pregnancy in patients with end-stage renal disease (ESRD) on chronic hemodialysis at the Mohammed VI university hospital center in Oujda, Morocco. The first case involved a patient whose pregnancy was managed up to 36 weeks of gestation, resulting in the delivery of a live newborn weighing 1600 gm. This outcome was achieved through careful control of blood pressure, management of dry weight, acceptable hemoglobin levels, and optimization of hemodialysis sessions. The second case was more complicated, involving a congenital malformation (omphalocele) that led to preterm labor at 25 weeks. The premature infant, weighing 600 gm, unfortunately died two hours after birth. This observational study highlights the challenges of managing pregnancy in patients on chronic hemodialysis and underscores the importance of multidisciplinary care to improve outcomes. A review of the literature is also provided to contextualize these findings.

Keywords: Pregnancy, Chronic hemodialysis, Conception, End stage renal failure

INTRODUCTION

Conception in women receiving dialysis is a rare event, with an incidence rate of 2.4% according to data from the American registry.[1] This rarity is due to dysfunctions of the hypothalamic-pituitary axis, which cause secondary amenorrhea and anovulatory cycles, making pregnancy precarious. Since the first reported pregnancy in a dialysis patient in the 1970s numerous studies have analyzed the frequency and outcome of pregnancies in this population, both in developed countries and in developing countries like Morocco.[2] This paper presents our experience with pregnancy in a chronic hemodialysis patient, comparing it with literature to analyze clinical and biological data, discuss maternal and fetal complications, and examine long-term maternal-fetal outcomes and factors favoring successful pregnancy.

CASE REPORTS

Case 1

Mrs. F.O, 26 years old, with a history of appendectomy and ESRD due to indeterminate nephropathy, has been on hemodialysis for three years, with a residual urine output of approximately 500 ml/24 h. This was her second pregnancy, with the first resulting in intrauterine fetal death at six months, delivered vaginally amid a hypertensive crisis. The patient maintained a diuresis of 900 ml/day. Since starting dialysis, her average blood pressure was 150/100 mmHg. Her pre-pregnancy treatment included amlodipine 10 mg and perindopril 5 mg. Her dialysis sessions proceeded without major incident, with hemoglobin levels around 9 gm/dl. After starting dialysis, she had irregular cycles for six months,

then regular menstruation. Three years later, she presented with morning sickness and a four-month amenorrhea, 36 months post-dialysis initiation. A pregnancy test was positive, and ultrasound confirmed a 21-week singleton pregnancy. Therapeutic adjustments were made, including stopping teratogenic medications (Perindopril), replacing Amlodipine and Perindopril with alpha-methyldopa 500 mg three times a day and nicardipine 50 mg LP twice daily, increasing dialysis sessions to 6 days/week, 3 hours per session, administering 100 mg/day acetylsalicylic acid, adjusting dry weight based on pregnancy progression, correcting anemia with injectable iron supplementation, ferrous fumarate orally, long-acting erythropoietin (Epoetin beta 75 µg), and 5 mg/day folic acid, achieving hemoglobin levels around 11 gm/dl by the end of the pregnancy. Obstetrical monitoring was instituted. The pregnancy progressed without incident except for some pelvic pain from the second trimester, managed with an antispasmodic (phloroglucinol/trimethylphloroglucinol) suppository.

The pregnancy progressed well with an unremarkable pregnancy assessment until 29 weeks + 6 days when a severe intrauterine growth restriction below the 3rd percentile with an estimated fetal weight of 1083 gm and high umbilical resistance index (0.85) was detected, along with preterm labor signs on ultrasound (cervical length 28 mm). After a negative infection workup, two doses of prenatal corticosteroids were administered, with repeated evaluations by tococardiography and Doppler recording of the umbilical and fetal cerebral arteries until 36 weeks when reverse flow in the umbilical Doppler and abnormal fetal heart rate recording indicated an emergency cesarean for fetal rescue.

Case 2

Mrs. B.Y, 32 years old, with ESRD due to indeterminate nephropathy, has been on hemodialysis for six years, with a history of a spontaneous miscarriage not curetted 12 years ago, coinciding with the start of hemodialysis. The diagnosis of her second pregnancy was made at 20 weeks + 1 day, with a dialysis duration before conception of 72 months and residual diuresis of less than 250 ml/24 h. An obstetric ultrasound detected a congenital malformation type omphalocele with intestinal and hepatic contents, with a collar of 22 mm, in a fetus with positive cardiac activity, measuring 19 weeks. During her pregnancy, the patient was on low molecular weight heparins 0.4 UI/day, acetylsalicylic acid 75 mg/day, and methyldopa 500 mg: 1 tab three times/day, with increased hemodialysis sessions from 3 sessions of 2 hours/week to 5 sessions of 2 hours/week.

The pregnancy progressed without incident until 25 weeks when the patient experienced preterm labor, resulting in the spontaneous birth of a 600 gm male fetus who died two hours post-birth due to respiratory distress in a very preterm newborn.

DISCUSSION

Fertility in women on chronic hemodialysis

Hormonal changes induced by chronic kidney disease

Anovulatory cycles and amenorrhea are common in patients with ESRD. An American study involving 76 women on dialysis found that only 42% had regular menstruation, while 59% had irregular menstrual cycles. Additionally, the average age of menopause onset was 47 years, compared to 50 years in a control population.[3]

In women on dialysis of childbearing age, central anovulation due to hypothalamic dysfunction is most often observed.[4] Blood concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are elevated, with an absence of the LH surge induced by estrogens. Moreover, progesterone levels are reduced. Approximately 70 to 90% of patients exhibit hyperprolactinemia, which contributes to anovulation by inhibiting GnRH secretion. This hyperprolactinemia is induced by hyperparathyroidism and decreased renal clearance of prolactin.[5] Therefore, therapy is initially directed towards optimizing dialysis administration, correcting anemia with recombinant erythropoietin, and managing secondary hyperparathyroidism with vitamin D.[5] Fatigue and psychosocial factors related to chronic illness also play a role, making psychological support crucial in management.

Initial nephropathy and iatrogenesis

Initial nephropathy and administered therapies may compromise fertility. In lupus cases, antiphospholipid syndrome reduces the frequency of viable pregnancies and uncomplicated pregnancies. The pathogenesis of antiphospholipid antibodies directly targets trophoblastic cells, mainly through pro-apoptotic, pro-inflammatory mechanisms, uncontrolled immunomodulatory responses, and thrombotic phenomena, which explain recurrent miscarriages.[6] Current first-line treatment is limited to low-dose aspirin (LDA) and low molecular weight heparin, with a failure rate of 30%.[6] In the case of vasculitis, there is no primary involvement of the reproductive organs in women. However, Pagnoux et al found that more than half of the cases of granulomatosis with polyangiitis exhibited hypogonadism symptoms, characterized by FSH levels exceeding twice the normal range.[7] Treatments for initial nephropathy, such as cyclophosphamide, may also impair fertility, with a dose-dependent decrease observed in 20 to 85% of women of childbearing age, with significant risk for cumulative doses exceeding 15 gm.[8]

Loss of libido

A decrease in sexual activity in patients undergoing hemodialysis has been observed, with only 40 to 50% of women under 55 having active sexual activity, and 36% of

sexually active patients using contraceptives.[9] This reduced libido may partly be explained by the deterioration of body image related to chronic illness and the presence of an added depressive syndrome.[10]

Epidemiological aspects of conception in hemodialysis

Pregnancy occurrence in women on hemodialysis remains rare in Africa, with rates varying between 0.3% and 7.14%.[2,11] In the Moroccan medical context, the average age of pregnancy onset in dialysis patients was 34 years, with an average of 76 months on dialysis.[11] In Tunisia, this average age was 35.6 years, with an average hemodialysis duration of 4 years (50.64 months).[12] A case of a full-term pregnancy was reported in a 38-year-old patient on hemodialysis for 42 months in Madagascar in 2003.[13] Our patients were younger, with a pre-conceptional dialysis duration significantly longer than reported in other studies (48 months for the first case and 72 months for the second case).

Clinical aspects of pregnancy in chronic hemodialysis

In our cases, the initial nephropathy was indeterminate. Chaker reported that 74% (14 patients) had indeterminate nephropathy in Tunisia.[12] The case reported in Madagascar involved ESRD due to nephroangiosclerosis.[13] In Rabat, Morocco, among 11 pregnancies in 8 women on chronic hemodialysis at CHU Ibn Sina, the initial nephropathy was unknown in 6 out of 8 patients.[11] Another study conducted at the Mohamed V military hospital in Rabat on 12 pregnancies found that nephropathy was indeterminate in half of the cases, chronic glomerulonephritis in one case, chronic tubulointerstitial nephropathy in two cases, and vascular nephropathy in one case.[14] To our knowledge, no studies have been conducted on the impact of initial nephropathy on pregnancy outcomes. The lack of specification of initial nephropathy in our cases raises questions about the accessibility and costs of additional tests in the Moroccan context.

Diagnosis and course of pregnancy in chronic hemodialysis patients

Women on hemodialysis often experience delays in pregnancy diagnosis due to irregular menstrual cycles. In our cases, diagnosis was also delayed, consistent with literature observations.[15] Pregnancy is often detected through symptoms suggestive of pregnancy, which may initially be mistakenly attributed to under-dialysis manifestations. However, during the interviews with our two patients, a 4-month amenorrhea was revealed. Given that diuresis was maintained in both patients, a urine test was performed. However, it is advised not to rely on it due to the difficulty in interpreting it due to possible elevated β-HCG levels associated with chronic renal failure.[16] Ultrasound confirmed the pregnancy. However, according to Chaker's series, the diagnosis was made in 9 cases (36%) by β-hCG measurement.[12] In Hadj's study in Morocco, all patients were anuric, and diagnosis was made by ultrasound in the presence of pregnancy symptoms.[11] In the Madagascar case, diagnosis was made incidentally after seventeen weeks of amenorrhea, during a pelvic ultrasound requested for pelvic heaviness, despite the persistence of menstruation.[13] Upon diagnosis of pregnancy, the dialysis modality was modified in our patients, with the frequency increased to 18 hours (3HX6) per week. According to Piccoli, the number of hours per week was closely related to prematurity and hypotrophy.[17] Intensive long-term dialysis could reduce residual diuresis and accelerate the loss of residual renal function.[18]

The pregnancy course did not experience major maternal complications for our two patients. Blood pressure was well controlled, averaging 150/100 mmHg, thanks to monotherapy and careful assessment of dry weight through alpha-methyl-dopa, intensified dialysis, and dry weight adjustment. This estimation remains primarily clinical, aided by the knowledge of normal physiological weight gain during pregnancy. The target hemoglobin in a healthy pregnant woman is 9 to 11.5 gm/dl.[19] Anemia was managed using erythropoietin and iron supplementation.

According to Hadj's study, half of the 8 patients included experienced worsening of pre-existing hypertension and required therapeutic abortion. Anemia was also corrected in some cases with blood transfusion and iron supplementation due to the high cost of erythropoietin.[11]

Maternal and fetal outcomes/prognosis

Pregnancy in chronic hemodialysis remains burdened by significant maternal and fetal morbidity and mortality. Similar to incidence, the prognosis of pregnancies in hemodialysis patients has improved in recent years, from a fetal survival rate of 23% in the 1980s to 68.4% according to a recent study conducted in Canada.[1,20]

Fetal prognosis largely depends on gestational age and birth weight. On average, birth weight is less than or equal to 2000 gm, as in our patient, whose birth weight was 1600 gm.[21] A Canadian study with 48 hours of weekly dialysis reported an average fetal weight of only 2418 gm in 5 patients.[22] These results are corroborated by a more recent study where the average weight was 2118 gm and gestational age was 34 weeks of amenorrhea with a weekly dialysis duration of 43 hours.[20] In the most significant studies, such as Luders et al the average term is 32 weeks of amenorrhea, and deliveries are often induced prematurely due to intrauterine growth retardation (IUGR) or maternal risk associated with severe hypertension and/or preeclampsia.[21] Luders found that primiparity was associated with a higher risk of fetal complications, regardless of preeclampsia, while the presence of residual diuresis was considered a favorable prognostic factor by Piccoli.[17,21] According to several authors, for high-risk pregnancies in dialysis patients, prolonging pregnancy beyond 38 weeks of amenorrhea is not recommended, as maternal-fetal risk increases progressively after this term. Delivery may be considered as soon as risks related to

prematurity decrease, usually after pulmonary maturation, from 34 weeks.[23] Despite notable improvements in fetal survival among hemodialysis patients, the prognosis remains less favorable compared to the general population.

Obstetric complications

Spontaneous abortions

Due to cycle irregularity, the frequency of amenorrhea, and often late pregnancy diagnosis in dialysis patients, early or late spontaneous abortions are often underestimated, and their evaluation remains challenging. In a series of 37 pregnancies in hemodialysis patients, Hou found that 75 to 80% of these pregnancies ended in spontaneous abortion, intrauterine death, or stillbirth.[1] The 30% abortion rate observed in our study is consistent with recent literature.[20]

Hypertension and preeclampsia

The incidence of hypertension, preeclampsia, and/or eclampsia remains high in hemodialysis patients, despite improvements in management strategies. Preeclampsia and eclampsia are associated with worse maternal and fetal outcomes and are common in these pregnancies. Preeclampsia incidence ranges from 28 to 63%, and in our study, there was no case of eclampsia.[1] Piccoli's studies also showed that almost half of patients with an initial diagnosis of chronic hypertension may evolve into preeclampsia.[17] The severity of hypertension is often underestimated; however, elevated systolic blood pressure values generally range between 150 mmHg and 180 mmHg.[24]

IUGR

IUGR remains a common complication due to placental insufficiency, with 20 to 50% of infants having a birth weight below the 10th percentile for gestational age.[20] Our patient with a birth weight of 1600 gm is consistent with this observation. Despite significant progress in the management of pregnancies in the hemodialysis patients, this complication remains a common challenge due to the pre-eclampsia, placental dysfunction, and the hypertension.

CONCLUSION

Pregnancy in chronic hemodialysis remains a complex and high-risk situation that requires meticulous management to optimize maternal and fetal outcomes. Despite significant improvements in recent years, challenges related to hormonal disturbances, fertility, and pregnancy management persist. Continued advancements in treatment and management strategies are crucial to improving outcomes for these patients.

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