

## Outcome of Pregnancy in Chronic Hemodialysis Patients: Single Center Experience

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Received: June 23, 2022

Published: July 14, 2022

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### Abstract

Pregnancy is an uncommon event in women with End Stage Renal Disease who are on maintenance hemodialysis treatment. This case series conducted at Prince Naif Dialysis Centre, Security Forces Hospital and Lehbi medical Centre (Riyadh, Saudi Arabia) was aimed to study the outcome of pregnancies among end-stage renal disease (ESRD) patients on maintenance hemodialysis. The purpose of these cases was to share our experience in managing pregnant women's who were on long term hemodialysis in our center from January 2014 to March 2022. Out of 5 cases, 4 of them had delivery of alive newborns and 1 had intrauterine death of the fetus. The average age of patients was 33.5 years. The average time from start of hemodialysis to become pregnant was 20 months. The average gestational age at diagnosis was 13.5 weeks. Modification in dialysis prescription was made in all patients from 3 times per week to six times per week. The average time at delivery was 35.4 weeks. The average weight of newborns was  $2342 \pm 458$  gram. In conclusion successful pregnancy is possible in hemodialysis patients if managed with vigilance and with close follow up with multi-disciplinary team.

**Keywords:** Pregnancy; End-stage Renal Disease; Hemodialysis; Outcome

### Introduction

The first pregnancy with a successful outcome in patients on hemodialysis (HD) was described in 1971 by Confortini, et al. [1]. Pregnancy is a challenging experience for women suffering from chronic kidney disease (CKD) and even harder in End Stage Renal Disease (ESRD) patients undergoing maintenance HD [2]. However better improvement in maternal and fetal care and continuous improvement in dialysis efficiency, frequency and support therapy allow them to reach previously inaccessible targets [3,4].

In the 1980's and 1990's the reported frequency of conception among ESRD patients of child bearing age on dialysis ranged from 1.5 conceptions over 100 patients per year in the United States [2] to 11 conceptions per year as reported by EDTA and the main national registries [5]. The Australian, New Zealand dialysis and

transplantation registry from 2001 to 2011 reported seven conceptions per year [6]. Souqiyeh, et al. in 1992 reported the higher numbers of pregnancies in Saudi Arabia [7]. In recent past studies mainly from single centers showed a successful pregnancy outcome in more than 70% cases [8].

Situation is improving with improvement in dialysis technology and the result reported in the literature suggest a favorable outcome for pregnancy [9]. In a recent case series reported by Luder, et al. from Brazil [10], the successful rate was 87%. The main reason in the success of pregnancy in recent years appears to be the intensified dialysis dosing throughout gestation [11].

Early diagnosis of pregnancy in ESRD patients requires careful attention. Irregular menstrual cycles, amenorrhea, nausea and elevated beta-subunit of human chorionic gonadotropin have been

observed in some patients with renal failure which may give a false-positive pregnancy test. Due to this, estimation of beta HCG in blood may be done if a dialysis dependent premenopausal patient complains abdominal symptoms and before abdominal radiography. Any suspicion of pregnancy in these patients should lead to further testing by ultrasonography to detect fetal cardiac activity. A late diagnosis delays the intensive antenatal care and reduces the successful outcome [12]. A successful pregnancy in woman on dialysis requires early diagnosis and collaboration among nephrologists, dialysis unit staff and obstetricians [13]. Centers have developed protocols based on factors affecting pregnancy outcome to standardize the care of pregnant dialysis dependent patients [14].

We report this case series comprising of management and outcome of pregnancies in 5 dialysis patients which were managed based on our institutional protocol.

## Methods

This case series conducted at Prince Naif Dialysis Centre, Security Forces Hospital and Lehbi medical Centre (Riyadh, Saudi Arabia) was aimed to study the outcome of pregnancies among end-stage renal disease (ESRD) patients on maintenance hemodialysis. The study was conducted with approval of institutional ethical review board (ERB) and all the patients given informed and written consent for inclusion in the study. Beta HCG in blood was measured in laboratory in premenopausal patients who complained of amenorrhea. Pelvic ultrasound was also done if beta HCG was positive and referred to obstetrician. We had an institutional protocol for management of pregnant dialysis dependent patients. The dialysis prescription was intensified to have six days per week/four hour per session until delivery, with appropriate increases being made to dry weight to help estimate fetal growth from second trimester onwards. Online Kt/V was maintained at a value of more than 1.4 and confirmed by laboratory tests. Dietary regime was liberalized in regard to protein intake to maintained serum albumin between 35-40 gm/dl. All the potential teratogenic drugs (including sevelamer, cinacalcet) were stopped once pregnancy was confirmed. Patients received Folic acid, multivitamins (B complex), phosphate binders (calcium carbonate) and vitamin D. Erythropoietin was administered to maintained hemoglobin between 10-12 gm/dl. Intravenous iron supplement was used to maintained iron saturation between 30-50% and ferritin level between 200-800

ug/l. Blood pressure was maintained in the acceptable range, especially avoid hypotension during dialysis. The patient had followed up with obstetrician in the hospital and plan agreed with patients regarding management of the pregnancy and delivery.

All the data was recorded on proforma. The data was entered in Microsoft excel and analyze. Numerical data was analyzed by mean  $\pm$  standard deviation.

## Results

This case series included 5 pregnant ESRD patients (Table 1). Their ages ranged from 27 years to 40 years (mean age:  $32.2 \pm 5.2$  years). Their dialysis vintage ranged from 6 months to 48 months (mean duration on dialysis =  $19.4 \pm 16.7$  months). All these patients were on thrice weekly high flux hemodialysis and achieving good clearance ( $Kt/V \geq 1.4$ ) before pregnancy. Pregnancy was confirmed by serum beta HCG and pelvic ultrasound. Four patients delivered healthy babies while one had intrauterine death of fetus. All the four newborns had APGAR score of 9 at birth. Of the four babies, three were females and one male. The birth weight ranged from 1670 gram to 2700-gram (mean =  $2342 \pm 458$ ). No congenital anomaly was detected on examination by the neonatologist.

The dialysis prescription and drugs were frequently adjusted during the pregnancy to keep the parameters in range (Table 2). No anticoagulant was used and clotting of extra-corporeal circuits was prevented by high blood flow ( $\geq 390$  ml/min) and half hourly saline flushing if the circuit showed signs of clotting. High flux dialysis (4 hours session for 6 days/week) resulted in good clearance and all the patients achieved both online and laboratory calculated Kt/V above 1.4. Serum calcium was maintained above 8.5 mg/dl with oral calcium supplements (calcium carbonate). Serum phosphate remained on lower side because of frequent dialysis. Patients were encouraged to increase their intake of dairy products containing high phosphate. Intravenous iron (Iron saccharate complex) and erythropoietin (Epoetin beta) were used to keep the hemoglobin above 10 gm/dl throughout the pregnancy. All the patients had Hb between 10-12 gm/dl (mean  $10.6 \pm 0.2$ ). Dialysate bicarbonate was kept at (mean 31 mmol/L) to avoid metabolic alkalosis.

Three patients required antihypertensive drugs to control their blood pressure in range of 120-130/70-80 mmHg. Two patients required 3 drugs while 1 patient required 3 drugs (Table 1).

Case number	1	2	3	4	5	Mean
Age (yrs.)	40	32	28	34	27	32.2 ± 5.2
Cause of ESRD	Polycystic kidney disease	Diabetic nephropathy	Chronic glomerulonephritis	Reflux nephropathy	Unknown	
Gravid, Para (G,P)	G <sub>4</sub> P <sub>3</sub>	G <sub>3</sub> P <sub>2</sub>	G <sub>8</sub> P <sub>3</sub> <sup>++</sup>	G <sub>2</sub> P <sub>1</sub>	G <sub>2</sub> P <sub>1</sub>	
Time on dialysis	6 months	18 months	48 months	9 months	16 months	19.4 ± 16.7
GA (weeks)	37	33	33	38	36	35.4 ± 2.3
Hypertension	No	Yes	Yes	No	Yes	
Anti-hypertensive Treatment	---	Methyldopa, nifedipine, hydralazine	Methyldopa, nifedipine	-----	Methyldopa, Labetalol	
Mode of delivery	SVD	IUFD	SVD	LSCS	SVD	
Birth weight (gram)	2500	-----	1670	2500	2700	2342 ± 458
Apgar 1 <sup>st</sup> and 5 <sup>th</sup> minute	9/9	-----	9/9	9/9	9/9	
Gender of baby	Female	-----	Female	Male	Female	

**Table 1:** Parameters of study women.

ESRD: End Stage Renal Disease; GA: Gestational Amenorrhea; LSCS: Lower Segment Caesarian Section; IUFD: Intra Uterine Fetal Death.

Case number	1	2	3	4	5
HD Frequency	6 times/week	6 times/week	6 times/week	6 times/week	6 times/week
HD Duration	4 hours	4 hours	4 hours	4 hours	4 hours
Kt/v	>1.4	>1.4	>1.4	>1.4	>1.4
Dialyzer size	170 H	170 H	140 H	170 H	170 H
Dialysate HCO <sub>3</sub> <sup>-</sup>	30 mmol/l	32 mmol/l	30 mmol/l	33 mmol/l	31mmol/l
Dialysate Na <sup>+</sup>	135 mmol/l	135 mmol/l	135 mmol/l	135 mmol/l	135 mmol/l
Dialysate K <sup>+</sup>	3.0 mmol/l	3.0 mmol/l	3.0 mmol/l	3.0 mmol/l	3.0 mmol/l
Heparin dose	None	None	None	None	None

**Table 2:** Dialysis Prescription.

HD: Hemodialysis, HCO<sub>3</sub> Bicarbonate, Na<sup>+</sup>: Sodium, K<sup>+</sup>: Potassium.

**Discussion**

Pregnancy in women with CKD has always been considered as a challenging event both for the mother and fetus. Over the period of study, we had 5 patients who conceived. The age of patients ranged from 27 years to 40 years (mean age 32.2 ± 5.2) which is close to 35.63 ± 5.62 years (range 23 to 44 years) reported from Tunisia [15]. It is also close to previous reports from Saudi Arabia [16]. All the patients had at least once conceived before start of dialysis. The

dialysis vintage ranged from 6 months to 48 months (mean 19.4 ± 16.7 months). There are better chances of successful pregnancy during earlier years after start of dialysis and fetal anomalies also increase with increasing dialysis vintage [17]. The exact cause is not known but may be due to increasing maternal age and vascular changes.

The gestational age ranged from 33 weeks to 38 weeks with mean gestational age 35.4 ± 2.3 weeks. This is in contrast to re-

port that around 40% pregnancies last more than 34 weeks [6]. Birth weight of neonates in our patients ranged from 1670 gm to 2700 gm while a study from Tunisia [18] showed average neonatal weight of 1970 Gm (range 1500-2300 Gm) and Yang, *et al.* [19] reported mean neonatal weight of  $1810 \pm 1193.8$  Gm. Our data shows that 80% (4 out of 5) pregnancies resulted in live births in contrast to 30% from Saudi Arabia<sup>7</sup> in 1992 and closely matching 79% reported by Yang [19] over the period from 1995 to 2009. One patient (25%) had intrauterine fetal death at 33<sup>rd</sup> week of gestation. There was no obvious reason for this loss. All the 4 neonates had APGAR score of 9/9 at first and 5<sup>th</sup> minutes while Yang, *et al.* [19] reported APGAR score of  $8 \pm 4$  at 5 minutes. Preterm infants with lower Apgar scores have an increased risk of neonatal death. Higher risk of mortality is seen among those neonates born at 36<sup>th</sup> weeks of gestational age or earlier [20].

Our dialysis center is corporate dialysis clinic and provides quality dialysis services achieving clinical performance parameters set by the company. We have a protocol for management of pregnancy in dialysis patients. The increased frequency and dosing of HD leads to decreased blood urea concentration and better control of volume and blood pressure. In the second and third trimester, the dry weight should be increased by 0.5 kg per week on the basis of patient blood pressure and intra uterine fetal weight assessed on ultrasound examination [10,13]. The dialysis regimen in each of our four patients increased to 6 days each week achieving a total dose of 24 hours that resulted in a blood urea nitrogen level less than 8 mmol/l and optimal blood pressure control (Table 2).

In pregnancy Hypertension is a common complication [14] and was found in our two patients. Better management of blood pressure control with adequate ultra-filtration and anti-hypertensive medications can decrease maternal complications and increasing the likelihood of successful delivery.

Pregnant women have a chronic respiratory alkalosis from hormonal stimulation of the respiratory center and lifting of the diaphragm by the enlarged uterus. The pregnant hemodialysis patients should be dialyzed against a lower bath concentration of bicarbonate to achieve a lower serum bicarbonate level to compensate this respiratory alkalosis [12,21].

Iron deficiency anemia is common in pregnant women especially in the third trimester as fetal demand for iron increases which

results in increase preterm delivery and subsequent decrease birth weight [22]. Thus, iron stores should be checked regularly and provide intravenous iron to prevent iron deficiency anemia. Anemia also results from the deficiency of erythropoietin which can be easily administered via intravenous or sub cutaneous routes. Our four patients responded to erythropoietin but with high doses to maintain hemoglobin in 10-12 gm/dl.

This is a small study but it gives encouraging results. Outcome of pregnancy can be improved by following a treatment protocol.

## Conclusion

The pregnancy outcome has improved in recent decades, but data on pregnancy outcome are limited due to the small sample size of previous case series. It is hard to draw firm conclusions from these sparse data. There are more than 20,000 patients on chronic dialysis in the kingdom of Saudi Arabia. Registry of pregnancy in dialysis patients is worth the effort to be created.

## Conflict of Interest

None.

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