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Case Series

Internal Medicine Section

# Successful Completion of Pregnancy on Maintenance Haemodialysis: Experience from a Resource-Short Model

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## ABSTRACT

Data pertaining to pregnancy completion on haemodialysis in Chronic Kidney Disease (CKD) patients from the developing world are scarce. We report three successfully completed pregnancies on Maintenance Haemodialysis (MHD) between January 2012 and June 2015 from two tertiary care hospitals in South India. A total of 58 women of child bearing age underwent MHD during the period of 42 months. Calculated conception rate per year was 1.47% for the period. Conception occurred in two patients while already on haemodialysis. The mean weekly duration of dialysis treatment was 18.75, 23.8 and 21 hours. Pregnancies were completed at 32, 34 and 33 weeks, with delivery of low birth weight infants 1.44, 1.27 and 2.3 Kilograms. All three patients were socioeconomically disadvantaged but could undergo enhanced dialysis with the support of locally generated funding in two cases and an insurance scheme for low income employees in the third.

**Keywords:** Chronic kidney disease, Outcomes, Socioeconomic status

Pregnancy is an uncommon event in CKD patients on haemodialysis. Hormonal milieu alterations resulting in impaired ovulation and sexual dysfunction lead to infertility in End Stage Renal Disease (ESRD) [1]. Improving conception rates on haemodialysis have been recorded world over since the first report in 1971 [2]. Conception rates overall in ESRD were as low as 2.2% in the 1990s [3]. Registry data from Australia and New Zealand have shown a higher number of pregnancies per year in ESRD patients in the decade 2001-11 than previously [4]. A recent United States national survey reported pregnancies ranging from 1-7% in women on chronic dialysis [5]. Live birth rates of 86.4% have been documented, although significant geographic variation remains [6].

Developing world data pertaining to pregnancy outcomes on haemodialysis are scanty and limited to case series and single case reports [7-9]. In India the expanding prevalence of ESRD and poor population penetration of dialysis compounded by resource scarcity has resulted in suboptimal delivery of CKD care [10]. Maternal and fetal outcomes in 51 pregnancies in Indian women with CKD have been described [11]. However, the sole patient in this cohort with an estimated Glomerular Filtration Rate (eGFR) <15 ml/min/1.73m$^2$ opted for medical termination of pregnancy.

## Case 1

A 32-year-old female with Takayasu Arteritis and a left branch renal artery stenosis as well as an occluded right renal artery along with an infrarenal abdominal aortic aneurysm was on haemodialysis for 3 years. Her first pregnancy completed 11 years back was complicated by severe Pregnancy-Induced Hypertension (PIH) and two subsequent pregnancies had resulted in abortions (medically terminated due to severe PIH in the first and missed abortion in the second). Pregnancy was confirmed after patient reported amenorrhoea for 16 weeks while undergoing haemodialysis. She received 5 hours haemodialysis three times per week until 20 weeks of gestation when it was escalated to 5 hours four times per week thereafter until delivery. Her clinical course was complicated by hyperemesis gravidarum. Blood pressure control was poor during the initial phase of pregnancy requiring the use of three antihypertensive medications; however with enhancement of haemodialysis fair control was achieved with 20mg per day of nifedipine. A healthy female baby with birth weight 1.44kg was delivered at 32 weeks gestation through a Lower Segment Caesarian Section (LSCS). The post-surgical period was uneventful except for transient paralytic ileus.

## Case 2

A 26-year-old female with biopsy proven chronic tubulointerstitial disease in 2007 was on conservative treatment until April 2014. During this period she conceived three times. The first pregnancy was terminated medically as requested by the patient in view of newly diagnosed renal disease, the second ended in preterm delivery complicated by early neonatal death and the third resulted in spontaneous abortion. She conceived again 4 months after the initiation of maintenance haemodialysis. At 18 weeks of pregnancy she required hospitalization for threatened abortion which was managed conservatively. In the 29$^{th}$ week of pregnancy she developed cystitis with Extended Spectrum Beta Lactamase (ESBL) producing *Escherichia coli* which responded to parenteral antibiotics. She was dialyzed for 6 hours 3-4 times per week until 24 weeks of pregnancy and 6 hours on alternate days thereafter. At 34 weeks of gestation a LSCS was performed to deliver a male baby weighing 1.27 Kg.

## Case 3

A 27-year-old female on follow up for Autosomal Dominant Polycystic Kidney Disease (ADPKD) with CKD was documented with severe anaemia and worsening renal function during the 6$^{th}$ month of her third pregnancy. Her previous two pregnancies had resulted in full term normal deliveries but were complicated by PIH. Haemodialysis was initiated in the 25$^{th}$ week of pregnancy and she was treated with 6 hours of dialysis 3-4 times per week. Gestational period was uneventful, culminating in the vaginal delivery of a healthy male baby with birth weight 2.3 kg at 33 weeks.

All three patients underwent dialysis using 1.4 m$^2$ biocompatible polysulfone high flux dialyzers with mean blood flow rates of 300

ml/minute and dialysate flow rates of 500 ml/minute. The usual dialysate composition included sodium 138 mEq/L, potassium 2 mEq/L, calcium 1.5 mmol/L and bicarbonate 35 mEq/L. In view of serum phosphate levels less than 1.5 mg/dl, likely due to enhanced solute clearance from prolonged dialysis, case 2 required addition of phosphate to dialysate in the final 3 weeks of treatment. Arteriovenous fistulae were used for dialysis access in all three patients.

The mean monthly haemoglobin, weekly Erythropoietin (EPO) requirement and antihypertensive medication requirement for the 3 months prior to delivery are summarized in [Table/Fig-1].

Case 1 underwent a successful living donor transplant one year after delivery and has normal graft function at present. Cases 2 and 3 are currently continuing on maintenance haemodialysis 12 hours per week. All three babies attained normal developmental milestones and are well at the time of this report. An informed consent was obtained for the publication of the details related to the cases.

| | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| Haemoglobin (g/dl)* | 8.4 | 7.16 | 7.2 |
| Erythropoieitin dose (IU/Kg/ per week)** | 145.45 | 260.8 | 100 |
| Number of antihypertensive medications*** | 1 | 1 | 2 |
| Weekly dialysis duration (hours) | 18.75 | 23.8 | 21 |
| Birth weight (Kg) | 1.44 | 1.27 | 2.3 |
| Declared monthly family income (INR) | <1500 | 10,000 | <1500 |

**[Table/Fig-1]:** Comparison patient parameters, birth weight and socioeconomic status.
* Mean Haemogobin last month of pregnancy.
**Mean Dose last month of pregnancy
*** Number of antihypertensive medications last 3 months of pregnancy

## DISCUSSION

We have in this series presented data on three successful pregnancies among 58 women of child bearing age group on haemodialysis between January 2012 and June 2015 in two tertiary care hospitals in North Kerala, India. Calculated annual conception rate for the cohort during this period was 1.47%.

Maternal survival on haemodialysis has been shown to improve over time. A recent survey showed no maternal mortality among >187 pregnancies on haemodialysis over five years [5]. There were no deaths in our case series. The risk of maternal hypertension and preeclampsia increases in CKD, related to impaired vascular responsiveness and hypervolemia. Preeclampsia rate of 44% was documented recently in survey [5]. Adequate ultrafiltration improves blood pressure as was seen in case 1 of the series. Antihypertensive medication requirement, a surrogate for blood pressure control, has remained low in all three [Table/Fig-1].

Intrauterine growth retardation, low birth weight infants, preterm delivery and uterine or neonatal death are known to be common in ESRD pregnancies [12]. Poor solute clearance in the mother is hypothesised to lead to fetal solute diuresis and polyhydramnios.

Augmented clearance of uremic toxins has been proposed as a strategy for improving pregnancy outcomes. Increasing dialysis duration is the key in this regard. A significant relationship between hours of dialysis per week and fetal outcomes was documented in a recent meta regression analysis [13]. The weekly mean duration of dialysis in the Toronto nocturnal haemodialysis cohort was increased from 36 to 48 hours after the diagnosis of pregnancy [14]. Patients in the Canadian Prekid registry were found to have received weekly dialysis of 43± 6 hours; significantly more than the 17±5 hours in the American Registry for Pregnancy in Dialysis (ARPD) patients [6]. The standard of care is considered to be intensive (>20 hours per week) dialysis currently. The most common haemodialysis prescription for pregnant women in the United States is 4- 4.5 hours per session 6 days per week [5]. All three patients in our series received enhanced haemodialysis with mean durations 18.75, 23.8 and 21 hours per week of dialysis in cases 1, 2 and 3 respectively. While this is an improvement from their baseline prescription of 12 hours per week, the longer duration of treatment achieved in Canadian patients were aimed for but could not be attained in all three patients, resulting partly from costs of treatment borne by patients.

Haemodialysis delivery remains the same for pregnant patients as it is for others. The use of biocompatible membrane filters, now the standard of care in many regions including ours, may be advantageous in reducing intra dialysis complications. Dialysate prescription alterations are often required. Dialysate potassium concentration may need modification for hypokalemia and bicarbonate may need titration for alkalemia. Longer dialysis may necessitate phosphate addition to prevent and treat hypophosphatemia as in case 2. Assessment of maternal dry weight needs to factor the estimated fetal weight gain.

Dedication of specialist "high-risk" obstetricians to the care of pregnant women on haemodialysis has been employed in large volume centers [6]. A multidisciplinary approach including obstetricians, nephrologists and allied services is mandated by the myriad issues encountered. Fetal well being can be influenced by dietary challenges such as ensuring adequate protein intake and avoidance of hypocalcaemia. Anaemia, a near ubiquitous pregnancy problem, becomes more pronounced in patients on haemodialysis and needs dose escalation of EPO. All three of our patients developed significant anaemia despite EPO dose enhancement [Table/Fig-1].

Data available from literature regarding pregnancy on Peritoneal Dialysis (PD) are considerably meager. Only two among 36 case series retrieved for a recent meta regression analysis on dialysis pregnancy outcomes pertained exclusively to PD [13]. Impaired transfer of ova to the fallopian tube as a result of the hypertonicity of PD dialysate and failure of implantation due to adhesions from previous peritonitis episodes have been suggested as reasons for decreased rates of conception.

Monitoring parameters on haemodialysis should include maternal heart rate and blood pressure in addition to fetal heart rate and uterine contraction. Intradialytic obstetric monitoring remains unavailable for a large number of patients even in resource replete patient care environments. Around 75% of participating United States nephrologists reported a lack of access to obstetric monitoring during haemodialysis [5].

Sparse or nonexistent public funding/insurance support for dialysis and infrastructure lacunae has curtailed optimal ESRD management in developing countries. Private facilities requiring direct patient payment form the mainstay of care provision in many regions but remain inaccessible to the majority. Increased availability of nongovernmental funding and innovative government schemes are ushering in changes in dialysis care provision in the state of Kerala in India [15,16]. All three patients in our series were socioeconomically disadvantaged. Self declared monthly household income was less than 1500 Indian Rupees for cases 1 and 3. Both patients had access to locally generated nongovernmental funding for treatment which partly subsidized the cost of dialysis. Out of pocket spending for medications and investigations as well as the incomplete coverage of treatment costs by external sources impaired the enhancement of dialysis treatment to desired levels. Case 2 had access to the Employee's State Insurance Scheme (ESIS) which covers the treatment expenses of low income (≤ Indian Rupees 15000/month) workers and their dependants.

Two of the patients reported here conceived while already on dialysis. Pregnancy outcomes have been reported to be better in women who start dialysis after conception [4]. A similar picture was noted in our patients, with case 3 who started dialysis while already pregnant having an uneventful pregnancy course on dialysis culminating in the delivery of a baby with a higher birth weight [Table/Fig-1].

## CONCLUSION

In summary, this case series reports our experience with the successful completion of pregnancy on haemodialysis, a rare event especially in environments hampered by the shortage of material resources. Improvements in health care funding can result in universal implementation of treatment protocols, ultimately leading to better outcomes including those for pregnancy on dialysis.

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