Renal replacement therapy for acute kidney injury in pregnancy

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Introduction

With the liberalization of abortion laws and improved obstetric care in developed countries, acute kidney injury in pregnancy is now an uncommon occurrence [1,2]. Current incidence rates range between 1% and 2.8% [2]. Acute kidney injury requiring renal replacement therapy (RRT) occurs in <1 in 10,000–15,000 pregnancies [1]. Subsequently, there is little to guide the management of such patients.

We describe a case of pyelonephritis in pregnancy that led to critical illness and acute kidney injury. It demonstrates pregnancy-induced anatomical and physiological alterations and their effect on diagnosis and management. It serves as a basis for discussion regarding the most appropriate form of RRT in this setting.

Case report

A 27-year-old previously well Indian female, 22 weeks pregnant, was admitted with fever, right flank pain and pyuria. Her pregnancy had been uncomplicated prior to admission, as had two previous pregnancies. Medications included folate and iron.

She was alert and orientated but appeared unwell. Her temperature was 39.8 °C. Blood pressure was 85/60. Abdominal examination demonstrated lower abdominal and right flank tenderness, and a gravid uterus corresponding to gestational age.

Investigations revealed an elevated white blood cell count [leucocytes 17.5 × 10⁹/l (18 × 10³/µl)], mild anaemia [haemoglobin 108 g/l (10.8 g/dl)], and thrombocytopenia [platelets 95 × 10⁹/µl (95 × 10³/µl)]. Peripheral blood smear showed changes of sepsis but no microangiopathy. Serum creatinine was 405 µmol/l (5.3 mg/dl). Urinalysis demonstrated haematuria, pyuria and low-grade proteinuria. Renal ultrasound showed mild bilateral hydronephrosis, more significant on the right side. No cause of obstruction was identified, and the scan was reported as consistent with physiological hydronephrosis of pregnancy. Obstetric ultrasound confirmed a normal 22-week-old foetus in no distress.

The patient was treated for urosepsis with Ampicillin (2g IV), but became progressively hypotensive despite fluid resuscitation. On repeat ultrasound, debris was seen in the renal pelvis, suggestive of infection. The asymmetric pelvicocalyceal dilation was judged pathological and a nephrostomy was inserted, confirming pyonephrosis. Urine, blood and nephrostomy drainage cultures grew Klebsiella sensitive to ampicillin, but an urticarial rash prompted an antibiotic change to aztreonam (1g I.V. bid). Recombinant activated protein C [drotrecogin alfa (Xigris®)] was commenced for severe sepsis. Inotropic circulatory support was required for persistent hypotension. Progressive oliguria and hypoxia from fluid overload necessitated intubation.

Intensive daily haemodialysis was initiated (6h/session) using a biocompatible high-flux dialyser with surface area 1.8 m² (Asahi Polysulfone Series, Japan). To avoid hypotension, lines were primed and dialysate temperature was set at 35.5 °C. Dialysate and blood flow rates were 500 and 300 ml/min, respectively. Dialysate composition was as follows: sodium 140 mmol/l (140 mEq/l), potassium 4 mmol/l (4 mEq/l), bicarbonate 28 mmol/l (28 mEq/l) and calcium 1.25 mmol/l (5 mg/dl). Systemic anticoagulation was with heparin, implemented with a 500-unit bolus followed by 500 U/h. The low dose was used because of additive anticoagulant effect of drotrecogin alfa. Folate dose was increased to 2 mg/day to account for dialytic removal.

With cautious ultrafiltration, haemodynamic stability was maintained at each dialysis run (Table 1).
Inotrope requirements gradually decreased. The patient was extubated on Day 5, and around this time, urine output spontaneously increased. Following the sixth haemodialysis, RRT was successfully ceased. The foetus remained stable throughout.

The patient remained in hospital for 20 days total, over which time renal function normalized. Creatinine was 41 \( \mu \text{mol}/\text{l} \) (0.5 mg/dl) at discharge. Subsequently, a healthy baby was delivered at term. CT scan following delivery showed no calculi or obstructing lesion, and nephrostomy was removed. Renal function remained stable.

Discussion

We present a case of pyelonephritis in pregnancy, a not uncommon occurrence. It is interesting for the development of acute kidney injury requiring RRT. It illustrates the complexities of diagnosis and management of pregnant patients in such a setting.

Bacteruria in pregnancy occurs with a frequency similar to that in non-pregnant women [3]. However, it progresses to pyelonephritis in up to 40% [5], due to pregnancy-related anatomic urinary tract changes. Kidney size increases slightly and dilatation of the ureters and renal pelvis occurs, more prominently on the right side [6]. Most of the dilatation is attributed to the smooth muscle relaxing effect of progesterone, although the relatively abrupt increase in dilatation at mid-pregnancy suggests ureteral compression from an enlarging uterus [7]. The disproportionate dilatation is from relative left ureteral protection by the sigmoid colon [6,7], and greater right ureteral compression by uterine dextrorotation and right ovarian venous plexus dilation [8]. The dilated system promotes urinary stasis and ascending infection.

Ultrasound interpretation can be difficult if a pathological cause of obstruction is not identified. Diagnosis often requires clinical suspicion, and identification of subtle clues for infection including pelvic debris.

Because acute kidney injury in pregnancy is now rare, literature on management is extremely limited. There are no reports available to guide RRT. Treatment principles tend to follow those used for non-pregnant patients with acute kidney impairment. We argue that reliance on experience in non-pregnant patients’ risks failing to account for the impact of the major physiological changes that accompany pregnancy, and should not be directly followed.

Pregnancy induces an 80% increase in renal plasma flow, leading to a 50% rise in glomerular filtration rate (GFR) [9]. Changes occur early and persist until term [10]. Creatinine clearance should be 30% higher than in non-pregnant women [9], resulting in a serum creatinine decrease from non-pregnant values by 20–30% [10]. Thus, pregnancy is a state of augmented renal clearance, meaning that ‘adequate’ RRT in a non-pregnant patient is likely inadequate in pregnancy.

Although not critically ill, pregnant women with end-stage renal failure on maintenance haemodialysis may be a better comparison group. Despite some improvements over the last three decades in fertility and successful pregnancies in this population, pregnancy remains uncommon and outcomes remain poor [11]. Only 42% of women requiring RRT have normal menses due to hypothalamic-pituitary-gonadal axis abnormality [12], and conception incidence rates are in the order of 2% [13]. When pregnancy does occur, outcomes are consistently poor, with high prematurity, polyhydramnios and foetal-growth retardation [14]. Less than 50% of pregnancies result in a surviving infant [11], suggesting a deleterious foetal effect of an azotemic intra-uterine environment.

The literature on techniques to improve outcomes remains sparse, but existing evidence suggests that successful pregnancies and improved foetal outcomes require intensified dialysis regimens [11,14,15]. Gangji et al. [15] reported resumption of ovulation and an uncomplicated pregnancy in a 31-year-old woman, 8 months after conversion from conventional intermittent haemodialysis to nocturnal haemodialysis. A U.S. survey of 344 pregnancies showed a non-significant trend towards improved gestational age and infant survival with dialysis >20 h/week [13]. Souqiyyeh et al. [16] found dialysis hours were significantly longer in pregnancies continuing beyond the 28th week, and a Belgian study of five patients correlated dialysis dose with infant birth weight [14].

We elected to perform daily, 6-h, intermittent haemodialysis, believing intensive dialysis would aid...
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urate clearance and best mimic normal pregnancy. The aim was normalization of biochemical parameters. Based on experience with nocturnal haemodialysis [17], we felt daily dialysis would minimize fluctuations in metabolic and electrolyte parameters, and allow enhanced clearance of small solutes and middle molecular weight compounds (Table 1).

Frequent dialysis was critical, given the haemodynamic instability of the patient. It allowed for lower ultrafiltration goals with each haemodialysis session, minimizing intra-dialytic hypotension and potential feto-placental circulation compromise. Conservative ultrafiltration goals were set, and our patient remained stable with no escalation of inotrope requirements at any stage.

Pregnancy is associated with a respiratory alkalosis, with a compensatory metabolic acidosis. Being ventilated and dialysed, our patient was at high risk of acid/base disturbance. We used a low bicarbonate dialysate [28 mmol/l (28 mEq/l), aiming for bicarbonate within the normal pregnancy range (18–20 mEq/l)] [11].

Requirements for water-soluble vitamins (particularly folate) increase during pregnancy, and losses increase with haemodialysis. Folate supplementation was escalated to 2 mg/day as recommended by Hou [18]. Also of concern was that increased dialysis would detrimentally lower potassium and phosphate levels. We measured serum potassium pre-dialysis and altered dialysate potassium concentration accordingly. We measured potassium and phosphate following dialysis and provided intravenous replacement as required.

Acute kidney injury in a critically ill patient is associated with high mortality. A critically ill pregnant patient is even more complicated, as a second patient, the fetus, is also involved. Maternal care should not be comprised, but simultaneously, safety of the foetus must be always considered. There is currently no literature to direct RRT in pregnant patients with acute kidney injury. Given the infrequency with which it occurs, it is unlikely there will ever be controlled trials or even reports of large series available. However, we believe that intensive daily dialysis achieves a physiological state as close to the normal pregnant state as possible, thereby providing a theoretical reason to justify its use. The positive maternal and foetal outcome in this case supports this approach. Increased reporting of similar cases is needed to validate our treatment approach.

Key messages

- Acute kidney injury in pregnancy is a rare occurrence. There is no literature available to guide RRT in this setting.
- Normal pregnancy is characterized by increased renal perfusion and GFR, making it a state of augmented renal clearance. What constitutes adequate RRT in the non-pregnancy setting is likely inadequate in pregnancy.
- Experience with pregnant women with end-stage renal failure on maintenance haemodialysis provides evidence that an azotemic intra-uterine environment has deleterious foetal effects. It suggests that increased uraemic clearance leads to an increase in successful pregnancies and better foetal outcomes.
- Daily, 6 h intermittent haemodialysis provides ‘intensive’ solute clearance and allows better haemodynamic stability, making it an appropriate form of therapy for acute kidney injury in pregnancy.

Conflict of interest statement. None declared.

References


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