**Two cases of Pregnancy in Patients with Cystinosis**

**Background :** Cystinosis is a rare autosomal recessive disorder which causes lysosomal accumulation of cysteine in all tissues; primarily the kidneys. Fanconi syndrome occurs at 6-12 weeks of life and renal glomerular cells undergo progressive damage leading to End Stage Renal Disease (ESRD) within the first decade. Transplantation restores renal function, and early initiation of cysteine-depleting therapy, cysteamine, delays development of ESRD and extra-renal complications including corneal crystal deposition, hypothyroidism, diabetes and muscle wasting. With improved life expectancy and restored fertility through kidney transplantation, pregnancy in cystinosis is now possible. Only six cases of pregnancy in cystinosis patients have been reported to date and little evidence is available regarding its management, so the evidence base requires expansion. We report two contrasting cases of pregnancy in cystinosis patients from our renal antenatal clinic; one with uncomplicated pregnancy and another with an adverse obstetric history and disease progression.

**Case 1:** 26-year-old female with ESRD secondary to cystinosis who received a living donor renal transplant in 2002 which was functioning well. Cysteamine was continued whilst trying to conceive but suspended after a positive pregnancy test. At 6 weeks’ gestation she commenced low dose aspirin due to the increased risk of pre-eclampsia conferred by chronic kidney disease and renal transplant. Pregnancy progressed well with normal transplant function and blood pressure. At 37 weeks, she delivered a healthy baby girl by elective Caesarean section. Cysteamine was restarted after delivery, and 1 year post-partum eGFR was 68 (comparable to pre-pregnancy renal function).

**Case 2:** 33-year-old female with cystinosis complicated by ESRD, hypothyroidism and corneal crystal deposition, and a history of recurrent early miscarriage. She received a cadaveric kidney transplant in 1998 and was also taking cysteamine pre-pregnancy. No structural causes for infertility were identified on pelvic ultrasound scan (USS) or hysterosalpingogram but she had previously tested borderline positive for lupus anticoagulant twice. After a positive pregnancy test, cysteamine was stopped and prophylactic aspirin and enoxaparin commenced in view of prior obstetric history. Vaginal bleeding and left iliac fossa pain at 7 weeks’ gestation prompted an USS which confirmed an ectopic pregnancy and she later underwent laparoscopic salpingectomy. Post pregnancy she experienced breathlessness and although thromboembolism was excluded, spirometry revealed a progressively worsening restrictive lung defect. This was likely due to respiratory muscle weakness secondary to cystinosis. Post-pregnancy eGFR was 31 (comparable to pre-pregnancy function).

**Discussion:** Uncomplicated pregnancy is possible, although rare, in cystinosis. Potential challenges related to pregnancy in cystinosis include cephalopelvic disproportion due to maternal short stature and impaired immunity due to lysosomal dysfunction which is further exacerbated by transplant immunosuppression. Cysteamine is stopped in pregnancy as it has been shown to be teratogenic in rats (1). However, without treatment, cysteine accumulates in the placenta which could adversely affect placental blood flow, and increase potential damage to other organ systems. The risk of accelerated progression to late complications of cystinosis is unknown, although omitting cysteamine for as little as 6 weeks post-transplant to maximise immunosuppressant absorption is considered too great a risk (2). Current practice is to stop cysteamine on confirmation of pregnancy, and not in the pre-pregnancy planning period, although more evidence is needed to better guide treatment decision-making. Long-term follow-up of patients with cystinosis who experience pregnancy is required to evaluate the effect of interrupting cysteamine treatment on disease progression.

**References:** 1.)Beckman DA, Mullin JJ, Assadi FK. Developmental toxicity of cysteamine in the rat: effects on embryo-fetal development. Teratology. 1998;58(3-4):96-102. 2.)Berryhill A, Bhamre S, Chaudhuri A, Concepcion W, Grimm PC. Cysteamine in renal transplantation: A report of two patients with nephropathic cystinosis and the successful re-initiation of cysteamine therapy during the immediate post-transplant period. Pediatr Transplant. 2016;20(1):141-5.