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Eculizumab in pregnant patients with Atypical Haemolytic Uraemic Syndrome (aHUS)

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Background
Atypical HUS is associated with mutations in the complement genes: CFH; CFI; CD46; C3 and CFB. These genetic mutations are not causative but are instead predisposing with aHUS unmasked by triggers such as infection or pregnancy. Historically the outcome of aHUS at the initial presentation was very poor, as were outcomes after kidney transplantation. The treatment of aHUS with Eculizumab has revolutionised the outcome for patients. Pregnancy and the post-partum was a particular risk period for aHUS however Eculizumab treatment has now been used in aHUS patients through pregnancy
Aim
The aim of this study was to analyse the UK experience of Eculizumab treatment in pregnant aHUS patients
Findings
Since the initiation of the national specialised aHUS service commissioned by NHS England in April 2013 ~750 individuals have been referred with suspected aHUS. 178 were females of child bearing age with 81 receiving Eculizumab treatment. In those who became pregnant on Eculizumab monitoring of AH50/CH50 demonstrated loss of complement blockade from the second trimester onwards requiring an increase dose of Eculizumab. Around 66% of pregnancies went to full term delivering a healthy baby; ~33% of pregnancies had pre-eclampsia/foetal loss despite adequate complement blockade.
Conclusion
Pregnancy was historically considered impossible in patients with aHUS due to poor outcomes to both mother and baby. Eculizumab is now used to facilitate successful pregnancies. Complement blockade should be monitored from the 2nd trimester onwards and Eculizumab should be increased to ensure adequate complement blockade. We report no known congenital abnormalities in the babies born to women receiving Eculizumab in this cohort. These patients are at high risk for pre-eclampsia because of their history of previous acute kidney injury and clinical or subclinical chronic kidney disease. Although some animal and clinical data have suggested a link between pre-eclampsia and complement activation, in clinical practice C5 blockade does not prevent pre-eclampsia in patients with aHUS.