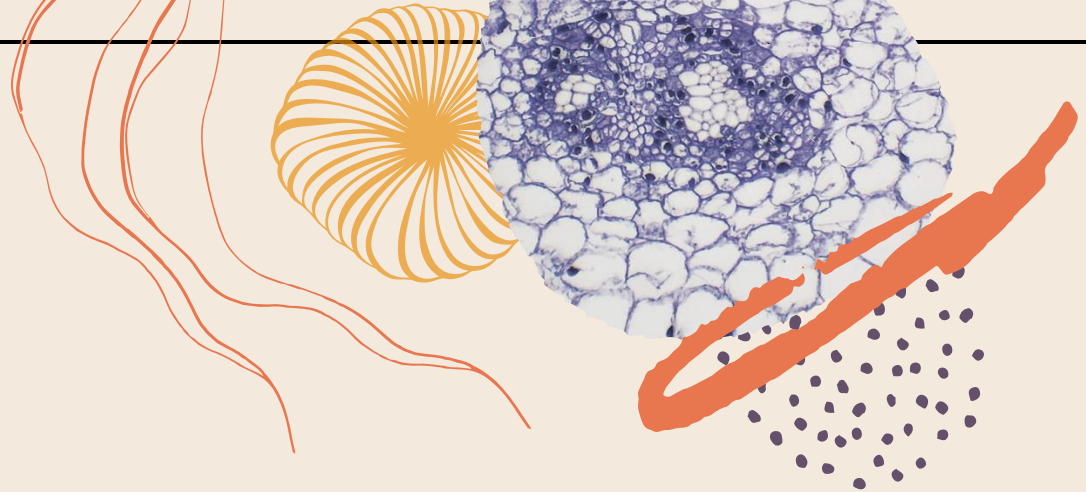

A Tug of War – A Case of Competing Priorities

ISOM / SOMANZ 2024 Challenging Clinical Cases

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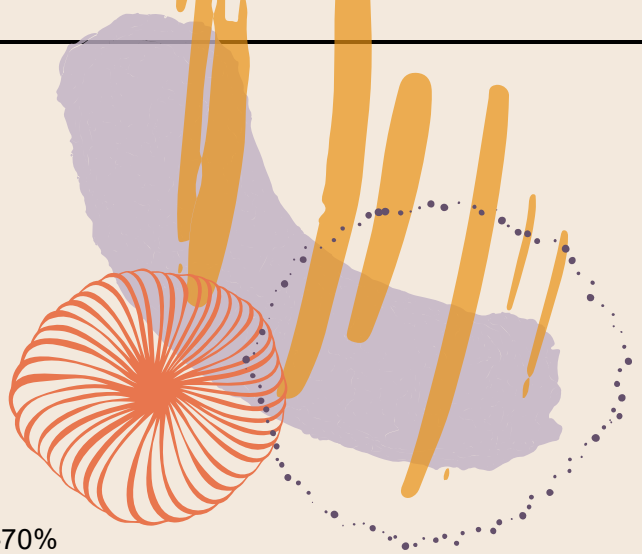
KC

- 33 F, Privigravida G1P0
- Spontaneous, planned conception



Complex Medical Background:

1. Cystic Fibrosis – Delta F508/C5052 DelA, on Trikafta

   - CF-related pulmonary disease, pseudomonas aeruginosa colonization, FEV 65-70%

   - Pancreatic insufficiency & gastroparesis (gastric emptying study)

2. Cystic Fibrosis-related diabetes mellitus – since 12 yo. Pre-pregnancy A1C 5.0%, DexCom CGM

   - Marked insulin deficiency at dx, 10-12 years of poor control in teenage years & early 20s (HBA1C 12-13%)

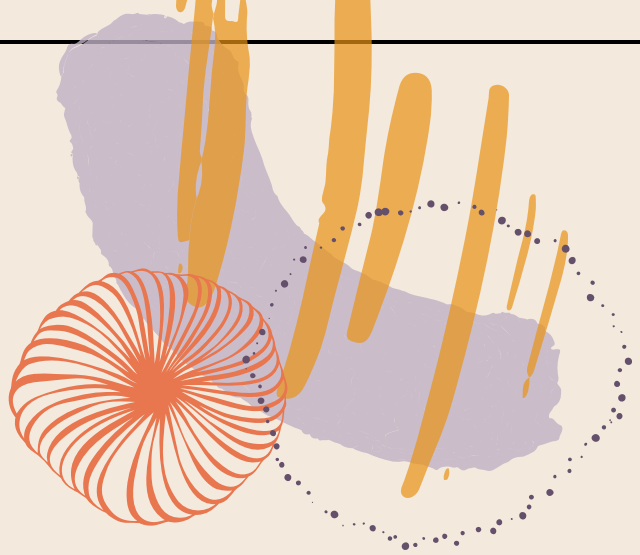
   - Retinopathy, macular oedema on intravitreal injection & nephropathy

3. Deceased Donor Kidney Transplant Nov 2022 – baseline creatinine 50-60mmol/L, right iliac fossa

   - presumed underlying diabetic and IgA nephropathy, HLA 6/6 MM, CMV +/-, EBV +/-, cPRA 0%

KC

Complex Medical Background (continued)



4. Chronic Hypertension
5. Previous Incidental TIA / CVA Feb 2021
6. Anxiety and Depression – previous steroid induced mood disorder post transplant and anxiety related to procedures / anaesthetics
7. Right frontal cavernoma – 1cm, under surveillance

Medications

1. Tacrolimus 1.5mg BD
2. Azathioprine 125mg mane
3. Prednisone 6mg daily
4. Labetalol 50mg to 100mg PRN TDS (self-titration)
5. Valaciclovir 500mg BD
6. Pantoprazole 40mg daily
7. Aspirin 100mg daily
8. Trikafta BD (Elexacaftor/Tezacaftor/Ivacaftor)
9. Insulin Detemir & Aspart (Levemir 30u/25u and Fiasp)
10. Duloxetine 60mg daily
11. Vitamin D 25mcg daily, Iron, Creon TDS, Multivitamin

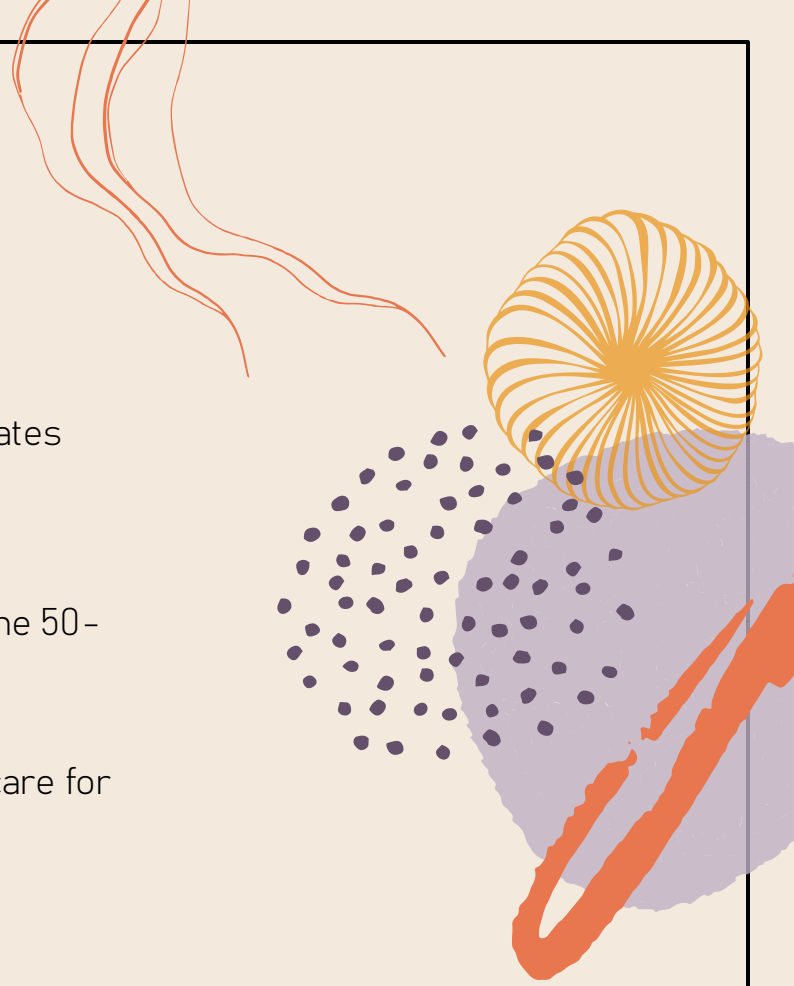
Early pregnancy

1st Trimester (0 to 13 weeks)

- Aspirin 150mg dose increment
- Mild hypertension BP 130-140mmHg, intermittently self titrates
- Tacrolimus level stable between 5 to 7
- Continuous Glucose Monitor – TIR 85% to 90%
- No proteinuria & renal graft function stable, serum creatinine 50-60mmol/L

- Managed by **Obstetric Midwifery Group Practice** midwifery care for continuity of care
- Frequent specialist clinic reviews on Q2-3 weekly basis

  (Renal, Respiratory, Gastroenterology, Obs Med)



Risk Stratification & Fetal Scans

13+2 weeks: 1st trimester risk scan

- Risk assessment based on: Maternal History, Mean Arterial Pressure, PAPP-A, PlGF, Uterine Artery Mean PI
- Risk for Pre-eclampsia before 37 weeks 1 in 1289

NIPT @ Low Probability

16 weeks: Early morphology scan

- AC 24%, EFW 31%, 164g.

Thoughts at this point??

Are we happy so far?

What concerns or risks should we be on the lookout for?

How frequently should we be reviewing KC?

Any particular fetal concerns or increased monitoring needed in the first trimester?

2nd Trimester (14 to 28 weeks)

17 weeks gestation:

- Rising blood pressures, 130-150mmHg systolic
  - commenced on regular labetalol
- Worsening nausea in pregnancy, gastroparesis
  - commenced regular Domperidone
- Moderate to severe constipation
- Insulin requirements: stable increase
  - Insulin detemir 80/30U, insulin aspart ICR 1u:7g with good TIR
- Stable renal graft function
  - serum creatinine 48-52mmol/L

- Tacrolimus level increased to 3mg / 2.5mg BD

- PET screening negative

Fetal Scans

<u>20 weeks: Morphology Scan</u>

- AC 52%, EFW 40%, 369g. Nil fetal anatomy abnormalities seen.
- Recommended 4 weekly scans

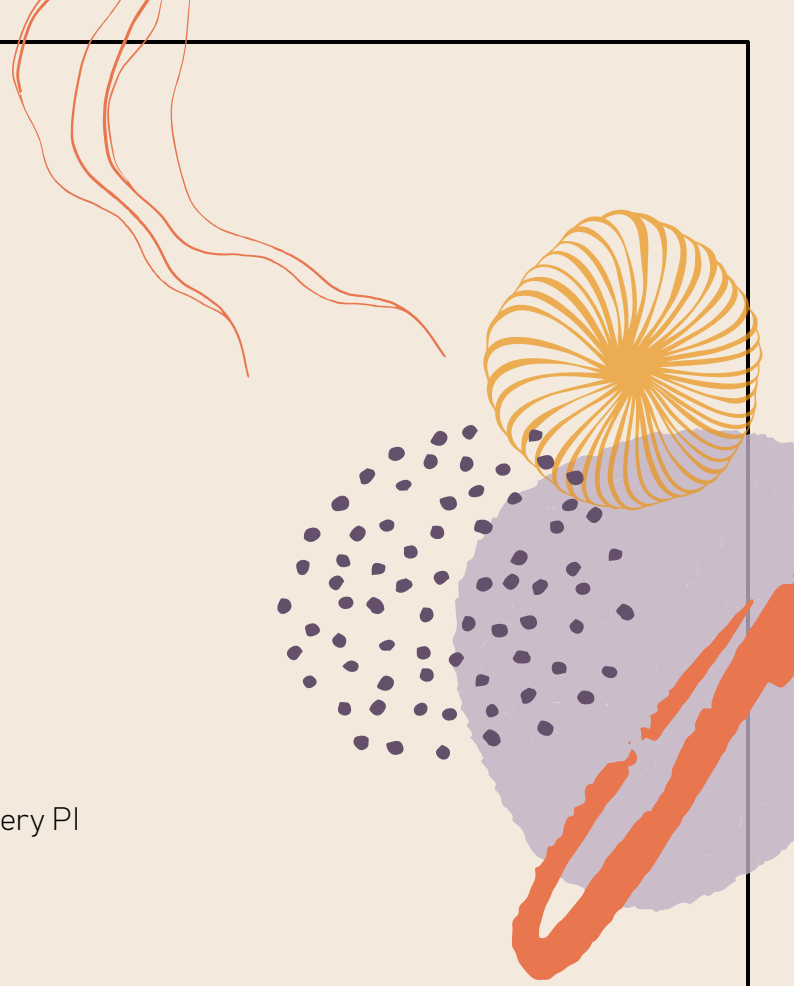
<u>25 weeks: Growth Scan</u>

- AC 78%, EFW 45%, 772g.

<u>28 weeks: Growth Scan</u>

- AC 67%, EFW 40%, 1169g. Normal AF measurement and umbilical artery PI

Overall satisfactory interval growth



Thoughts at this point?

Could you please comment on the utility of PET screening during the second trimester in this patient?

Are there any additional fetal surveillance recommendations given the history of CF, insulin-requiring DM, chronic HTN, renal transplant, etc?

Midwives are integral to the care of women during pregnancy, could you comment on their role in this case?

3rd Trimester (28 to 40 weeks)

Discussion in High Risk MDT meeting re: planning towards elective CS (patient's wishes)

- ensure discussion with transplant surgery

3rd Trimester (28 to 40 weeks)

29+6 weeks: Onset of significant pruritus

- serum Bile Acids of 39
- ICP diagnosed, commenced on Ursodeoxycholic Acid 250mg TDS
- Weekly review & monitoring of BP, BA and LFTs

- **Supratherapeutic Tacrolimus level > 9** with serial dose reduction required from 3.5/3mg to 2.5mg BD

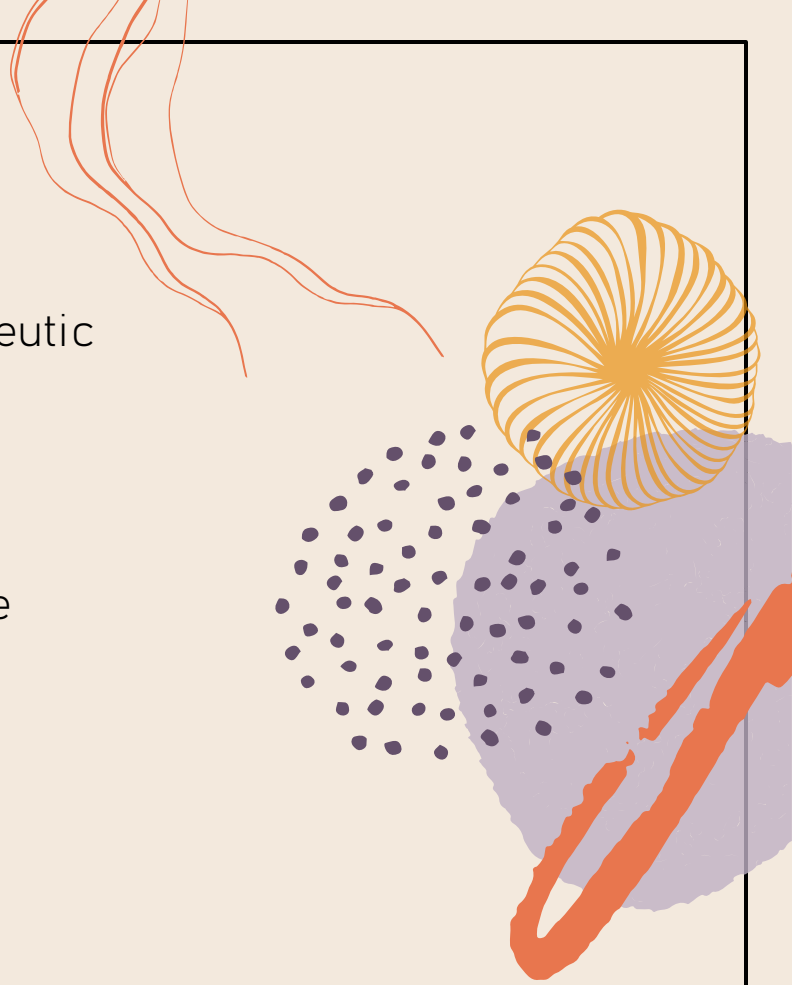
? Effect of Tacrolimus or cholestasis of pregnancy

Gestation	Bile Acids	Tacrolimus Level
26+0	-	4.4
26+6	-	5.8
27+6	-	5.7
29+0	-	7.5
29+4	11.9	8.3
29+6	39.9	9.1
30+2	41.8	9.9
30+6	49.4	8.7
31+2	72	6.7
31+6	82	6.1

Discussion

Is there a relationship between the supratherapeutic tacrolimus level and Intrahepatic Cholestasis of pregnancy?

Is there any information to date that may change your current management approach?



3rd Trimester (28 to 40 weeks)

31 weeks gestation admitted to hospital for a few reasons:

- Home BP control more erratic – SBP 170-200mmHG, admitted for inpatient monitoring & management

- Tacrolimus levels remain high despite serial dose reduction

- Despite higher tacrolimus level -> stable renal graft function

Gestation	Tacrolimus Level	Serum Creatinine (umol/L)
27+6	5.7	52
29+0	7.5	53
29+4	8.3	55
29+6	9.1	56
30+2	9.9	58
30+6	8.7	62
31+2	6.7	60
31+6	6.1	69

3rd Trimester (28 to 40 weeks)

- 31+2 weeks:
- Progressive rise in **serum creatinine** & new onset of **proteinuria** day 3-5 of inpatient admission

Gestation	Tacrolimus Level	Prot/Cr Ratio (g/mol)	Serum Creatinine (umol/L)
31+2	6.7	36	60
31+6	6.1	58	69
32+1	7.6	48	85

31+1 weeks U/S:
AC 53%, EFW 25%, 1622g
Umbilical artery EDF
Positive

? Tacrolimus toxicity vs Pre-eclampsia

Discussion

Can we differentiate proteinuria & worsening chronic hypertension from pre-eclampsia versus tacrolimus toxicity?

Does the SFlt1/PlGF ratio has a value in this situation?

Is the use of the ratio validated in this group of patients?

Discussion

PRE-ECLAMPSIA BIOMARKERS

sFlt1	12477	ng/L	( )
PlGF	83.5	ng/L	( )
sFlt1/PlGF ratio	149.5		( )

Comment:

sFLT1/PLGF ratio after 24 weeks gestation:
< 38 has a high negative predictive value after 24 weeks gestation.
> 85 is considered an aid in the diagnosis between 24 and 28 weeks.
(Pregnancy Hypertension 2020;20:44-49, NEJM 2016;374:13-22)

Reference intervals: (singleton pregnancies)

Gestation weeks	sFLt1 (ng/L)	PLGF (ng/L)	sFLt1/PLGF
14 - 19	750 - 2600	40 - 350	5 - 26
20 - 24	630 - 4500	180 - 870	1 - 17
25 - 28	600 - 4000	150 - 1000	1 - 9
29 - 33	700 - 3700	70 - 1200	1 - 35
34 - 36	1000 - 8500	40 - 750	2 - 158
> 36	1000 - 7500	40 - 750	2 - 131

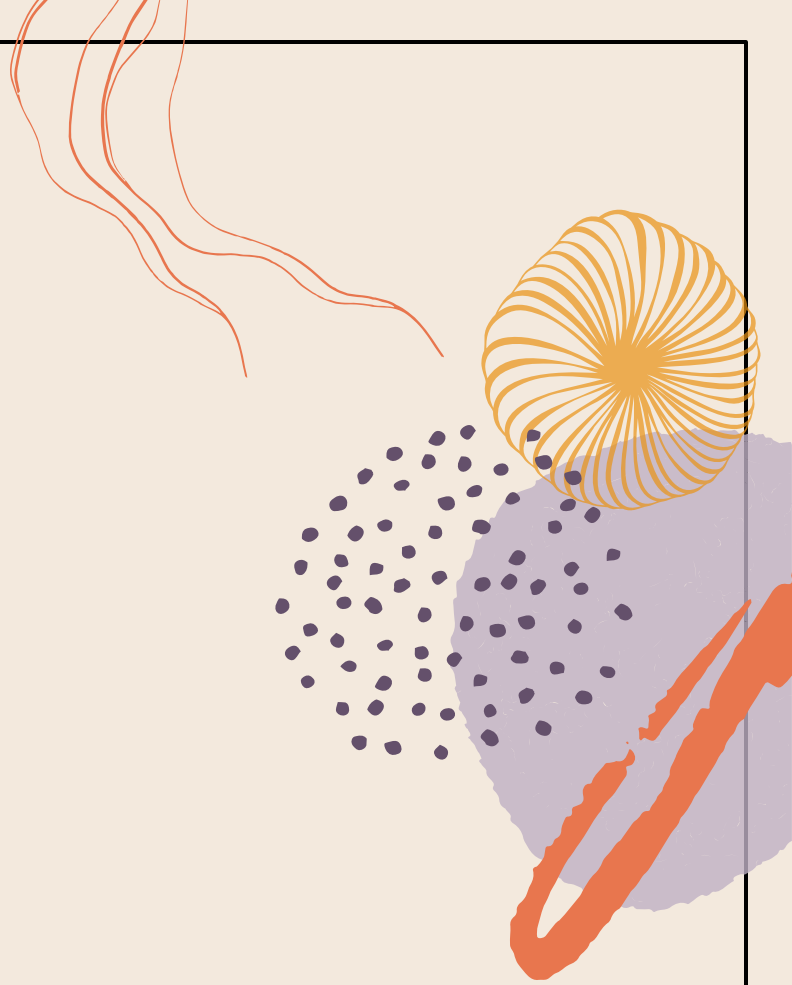
Discussion

Does this result change your thinking?

Based on the information we have, what would be your thoughts be relating to recommendations on inpatient vs outpatient management / disposition?

Delivery timing recommendations?

Indications / thresholds for delivery?



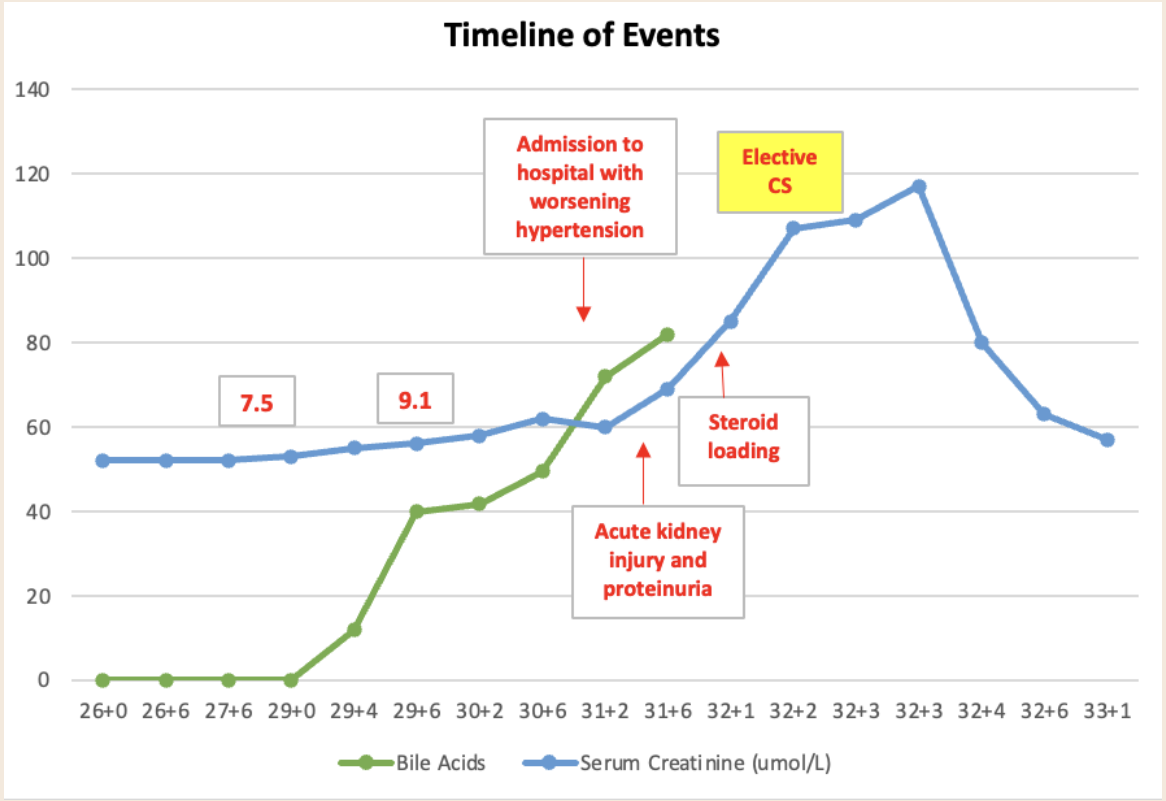
Progress

32 weeks: Multiple urgent reviews for hypertension SBP 150-170mmHg (with escalation in doses of 2 antihypertensive agents)

Progressively worsening renal function

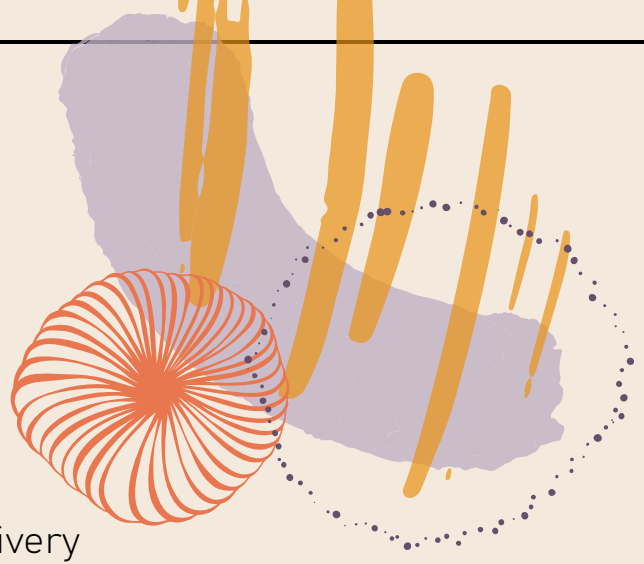
Gestation	Tacrolimus Level	Prot/Cr Ratio (g/mol)	Serum Creatinine (umol/L)
31+2	6.7	36	60
31+6	6.1	58	69
32+1	7.6	48	85
32+2	-	-	107
32+3	-	-	109
32+3	5.6	21	117

Steroid loading commenced at 32 weeks



PPROM at 32+1 weeks, elective CS on at 32+2 weeks

Postpartum



- Renal function returned to baseline
  - Serum creatinine 55-60umol/L within day 3-5 post delivery
- Postpartum mood disturbance and dissociative event
- Regular breastmilk supply by weeks 2-3
- Baby progressed well & discharged home at 6 weeks

Discussion

Postnatally, are there specific concerns you would like to address?

Any final points for consideration?

Thank you.