

Background

Addison's disease rarely presents de-novo during pregnancy. We highlight two cases diagnosed within a 3 month period at our centre

Case 1

A 41-year-old with mild depression treated with Sertraline presented at 11-weeks' gestation with an 8-week history of fatigue, weight loss, dizziness and nausea and vomiting.

Persistent hyponatraemia was noted (Na 122–127mmol/L) and random cortisol levels were 298–428nmol/l. She also had negative adrenal antibodies.

Sertraline withdrawal and fluid restriction at another centre did not improve her hyponatraemia and initially the use of synacthen was deemed contraindicated. As she had negative antibodies and adequate random cortisol levels, adrenal insufficiency was felt to be unlikely.

On transfer to our service, she was unable to stand (lying BP 88/53). Whilst being resuscitated with IV fluids, she had a short synacthen test performed, followed by immediate hydrocortisone administration. Her blood results came back later and the relevant investigations are demonstrated in Table 1.

As her 60 min cortisol was below the accepted first trimester pass cut-off of 700 nmol/l, she was continued on hydrocortisone treatment. As she had subclinical hypothyroidism with positive anti-TPO antibodies, levothyroxine was also commenced.

Marked clinical improvement was seen following appropriate in-patient resuscitation.

She was subsequently clinically and biochemically stable on hydrocortisone, fludrocortisone and levothyroxine. She has required significant psychological and pharmacological input for her depression and chronic disease diagnosis acceptance during pregnancy. She delivered a healthy baby at term. She required extra hydrocortisone during the 3rd trimester and has also required more frequent hydrocortisone to cover for breastfeeding overnight.

Her adrenal function was reassessed 3 months post partum and this time showed a completely flat SST as demonstrated in Table 2. Interestingly her repeat adrenal antibody test post partum was positive

Table 1

Investigations – December 2017	Patient 1
0 min cortisol	338 nmol/l
60 min cortisol	466 nmol/l
ACTH	67.8 ng/L (7.2 – 63.3)
Renin	16 (0.5 – 3.5)
Aldosterone	< 60 pmol/l
Na+	125 mmol/l
TSH	4.4 mIU/L
ft4	15.7 pmol/L
Anti-TPO	170 (positive)

Table 2

Ix – October 2018	Patient 1
0 min cortisol	< 28 nmol/l
60 min cortisol	< 28 nmol/l
Adrenal Ab	Positive

Table 3

Ix	Patient 2
0 min cortisol	114 nmol/l
60 min cortisol	125 nmol/l
ACTH	1515 ng/L (7.2 – 63.3)
Renin	6.9 (0.5 – 3.5)
Aldosterone	310 pmol/l

Case 2

Separately, a 36-year-old was referred to Bristol Dental Hospital at 8-weeks' gestation with a sublingual lesion and noted to have buccal pigmentation. She had few symptoms apart from fatigue and had been receiving compliments for her 'winter tan' for months.

Her random cortisol was 146 nmol/l. An SST confirmed adrenal insufficiency (Table 3)

On treatment with hydrocortisone and fludrocortisone, she progressed well through pregnancy. She also required higher doses of hydrocortisone in the third trimester. She delivered a healthy baby at 39 weeks and has returned to normal doses of hydrocortisone.

Discussion

These cases highlight the need for a high degree of clinical suspicion to diagnose Addison's in pregnancy. The presenting symptoms of vomiting and postural hypotension can often overlap with normal features of pregnancy. The majority of women with primary adrenal insufficiency will have normal pregnancy outcomes but there is an increased mortality and morbidity if undiagnosed. Some women will need an increase of 25 – 30% in their hydrocortisone doses during the 3rd trimester and a clear delivery plan for hydrocortisone treatment is needed. They may also require extra hydrocortisone to support breastfeeding overnight.

During normal pregnancy, there is a progressive increase in CRH and ACTH, with a gradual increase in CBG stimulated by oestrogen.

Insufficient trimesteral morning levels <300, <450, <600nmol/l should alert to a possibility of adrenal insufficiency (Lebbe 2013).

Synacthen can be used safely but there is a need to appreciate trimester specific cut-offs due to increasing CBG driving higher total cortisol levels in pregnancy. Table 4 illustrates the recommended pregnancy specific trimester 60 minute cortisol 'pass' levels for an SST.

Table 4

Trimester	Normal 9am cortisol (nmol/l)	60 min SST cortisol 'pass' (nmol/l)
First trimester	>300	>700
Second trimester	>450	>800
Third trimester	>600	>900

Reference:
 What is the best diagnostic and therapeutic management strategy for an Addison patient during pregnancy? [Lebbe M¹, Art W. Clin Endocrinol \(Oxf\).](#) 2013 Apr;78(4):497-502. doi: 10.1111/cen.12097