58 Year-old Male with Alcoholic Cirrhosis Presents with Hyponatremia

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11/8/12

HPI

- Fluid leaking from umbilical hernia secondary to his ascites
- Went to OR for drain placement which was complicated by hepatorenal syndrome
- Kidney function improved after 10 days and he was discharged home with follow-up with transplant clinic for eval for liver transplant

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2 weeks later

- Admitted from clinic for acute on chronic kidney injury
- He has had a history of hyponatremia with Na ranging from 128-132
- Morning of discharge, underwent cosyntropin stim which was abnormal, endocrinology consulted

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Symptoms

- No orthostasis, weakness,
- No anorexia, lethargy
- No nausea or vomiting
- No hyperpigmentation, salt craving
- No palpitations, no pre-syncope
- No AMS per family
- Occasional shortness of breath depending on his ascites. Feels much better after paracentesis.

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PMH

Alcoholic cirrhosis

CKD (GFR 40-50)

PSH

Lower back surgery

Umbilical hernia

Meds: Lasix 40 mg daily,
Ativan 1 mg daily,
Nadolol 40 mg daily,
Aldactone 25 mg daily

FH

Father: HTN, CKD

Mother: DM2

SH

Abstinent of EtOH since admission

No Tobacco

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Physical exam

Vitals: 36.2 121/53, 69, BMI 26, 96% RA

HEENT: mild scleral icterus

CV: RRR, no murmurs

Pulm: CTA bilaterally

GI: soft, +ascites, no rebound or guarding

MSK: 1+ LE edema

Neuro: A+Ox3, no asterixis

Skin: no hyperpigmentation but mild icterus

Psych: normal mood

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Initial Labs HD #1

131	103	3
4.6	22	1.5

90

9.0

5.9 76

25

6.2	3.2
3.5	63
31	14

INR 1.9

U_{Na} 15

8AM Cortisol 5.2→12.8→18.3

MELD score: 22

Child score: 10, class C

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Post Discharge Day #1 Labs

8AM Cortisol 5.9 mcg/dL, ACTH 29.2

8AM Fr Cortisol 1.07 mcg/dL (RR 0.07-0.93)

TSH 3.07 (RR 0.3-4.0)

FT4 1.08 (RR 0.9-1.7)

Seen in endo clinic 2 weeks after discharge.

Hemodynamically stable, no symptoms of adrenal insufficiency. Not started on steroids.

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Clinical Questions

- Assessment of adrenal insufficiency in cirrhosis?
- Effect of corticosteroid therapy in critically ill patients with cirrhosis?
- Etiology of hyponatremia in cirrhosis?

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Total Cortisol in Cirrhosis

- 90% serum cortisol is bound to albumin (20%) and CBG (70%)
- Reduction in these proteins are associated with a reduction in the bound-cortisol fraction.
- Serum total cortisol could be lower without having a low free biologically active hormone.

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Adrenocortical Dysfcn in Cirrhosis

- AI reportedly found in 40-48% patients with variceal bleeding and 26-64% w/ascites
- Hepatoadrenal syndrome: inadequate glucocorticoid activity w/respect to the severity of illness
  - Glucocorticoid resistance in inflammation
  - Decreased HDL levels→decreased steroidogenesis

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Adrenocortical Dysfcn in Cirrhosis

- 250 mcg Cosyntropin is recommended to diagnose AI in critically ill
- Serum total and plasma free cortisol were used to study 43 clinically stable cirrhotics.
  - Prevalence of AI
    - 39% w/standard criteria (peak total < 18mcg/dL)
    - 47% w/CIRCI criteria (Δ cortisol < 9mcg/dL)
    - 12% w/free cortisol (peak plasma < 1.2mcg/dL)
- Free cortisol index: total cortisol/CBG
- LDSST
- Salivary Cortisol

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Corticosteroid Use in Cirrhosis + Critical Illness

Outcome	Hydrocortisone *n = 39*	Placebo *n = 36*	Relative risk (95% CI)	*p* value
Mortality				
28-day mortality, no. (%)	33 (85)	26 (72)	1.17 (0.92 to 1.49)	0.19
ICU mortality, no. (%)	24 (62)	24 (67)	0.92 (0.66 to 1.30)	0.64
Hospital mortality, no. (%)	34 (87)	32 (89)	0.98 (0.83 to 1.16)	0.82
Hemodynamic response				
Change in norepinephrine infusion rate (day 2 – day 1), µg/kg per min, mean (SD)	–0.08 (0.22)	0.09 (0.28)	–0.17 (–0.28 to –0.05)*	0.005
Change in norepinephrine infusion rate (day 3 – day 1), µg/kg per min, mean (SD)	–0.16 (0.29)	0.11 (0.32)	–0.27 (–0.40 to –0.12)*	0.0006
Shock reversal, no. (%)	24 (62)	14 (39)	1.58 (0.91 to 2.55)	0.05
Vasopressor-free days, mean (SD)	6.8 (7.9)	5.6 (8.9)	1.2 (–2.7 to 5.1)*	0.54
Other outcomes				
Ventilation-free days, mean (SD)	6.7 (7.7)	8.1 (10.9)	–1.4 (–5.8 to 2.9)*	0.51
Renal replacement therapy-free days, mean (SD)	6.7 (7.8)	6.4 (10.6)	0.2 (–4.0 to 4.5)*	0.92
ICU length of stay for ICU survivors, d, mean (SD)	9.2 (6.4)	9.6 (6.0)	–0.4 (–5.4 to 4.5)*	0.86
Hospital length of stay for hospital survivors, d, mean (SD)	27.2 (12.8)	43.3 (34.0)	–16.1 (–54.5 to 22.4)*	0.90
Complications				
Shock relapse, no. (%)	14 (36)	5 (14)	2.46 (0.98 to 6.21)	0.03
Arrhythmia, no. (%)	10 (26)	6 (17)	1.54 (0.62 to 3.80)	0.34
Gastrointestinal bleeding, no. (%)	13 (33)	4 (11)	3.00 (1.08 to 8.36)	0.02
Hyperglycemia > 10 mmol/L, no. (%)	34 (87)	25 (69)	1.26 (0.98 to 1.61)	0.06
Ventilator-associated pneumonia, no. (%)	8 (21)	3 (8)	2.46 (0.71 to 8.57)	0.14
ICU-acquired bacteremia, no (%)	14 (36)	15 (42)	0.86 (0.49 to 1.52)	0.61

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Causes of death in Cirrhosis + Septic Shock

	Group 1 (n = 25)	Group 2 (n = 50)	P
Refractory shock (n)	0	20	.001
Type-1 hepatorenal syndrome (n)	2	3	NS
Liver failure (n)	4	4	NS
Variceal bleeding (n)	0	4	NS
Fungal infection (n)	2	0	NS

Group 1- adrenal function assessed, IV hydrocortisone if AI (17 patients- 68%)

Group 2- no assessment of adrenal function, no IV hydrocortisone

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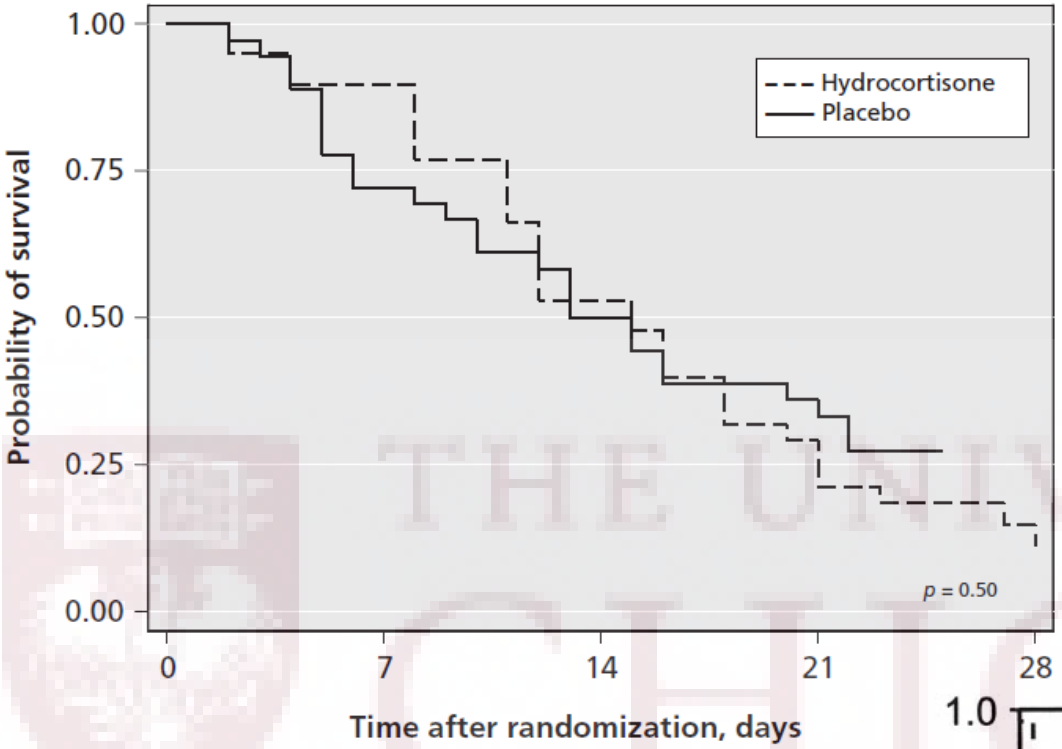
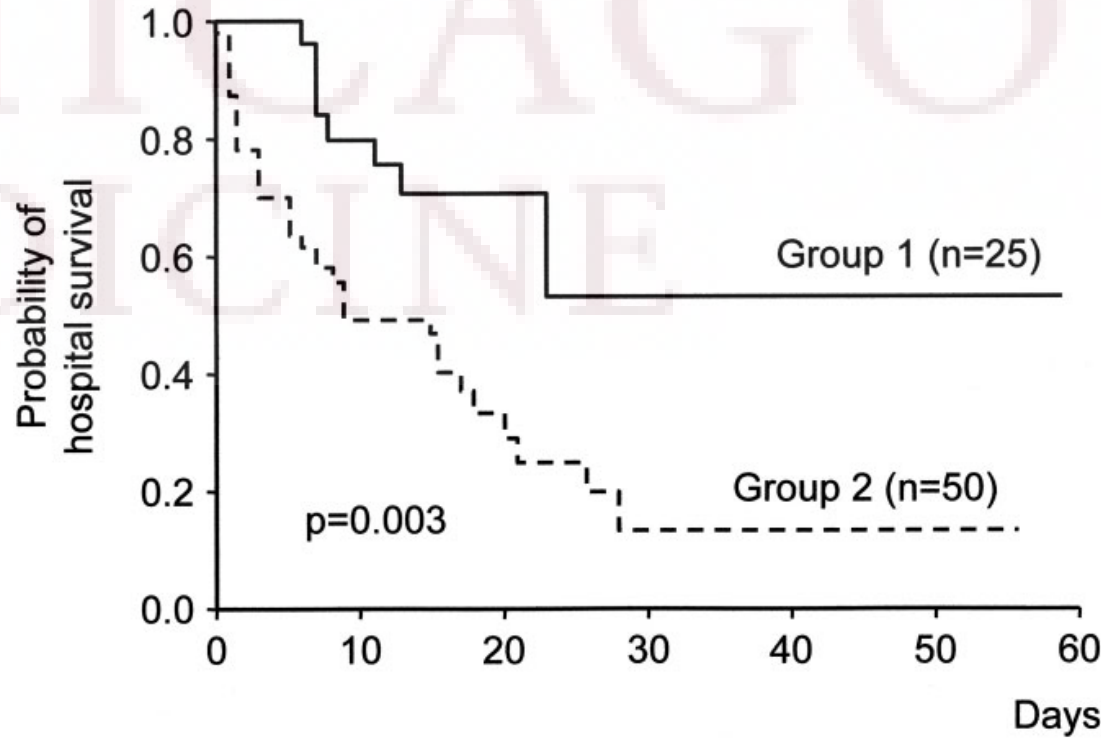


Corticosteroid therapy is controversial



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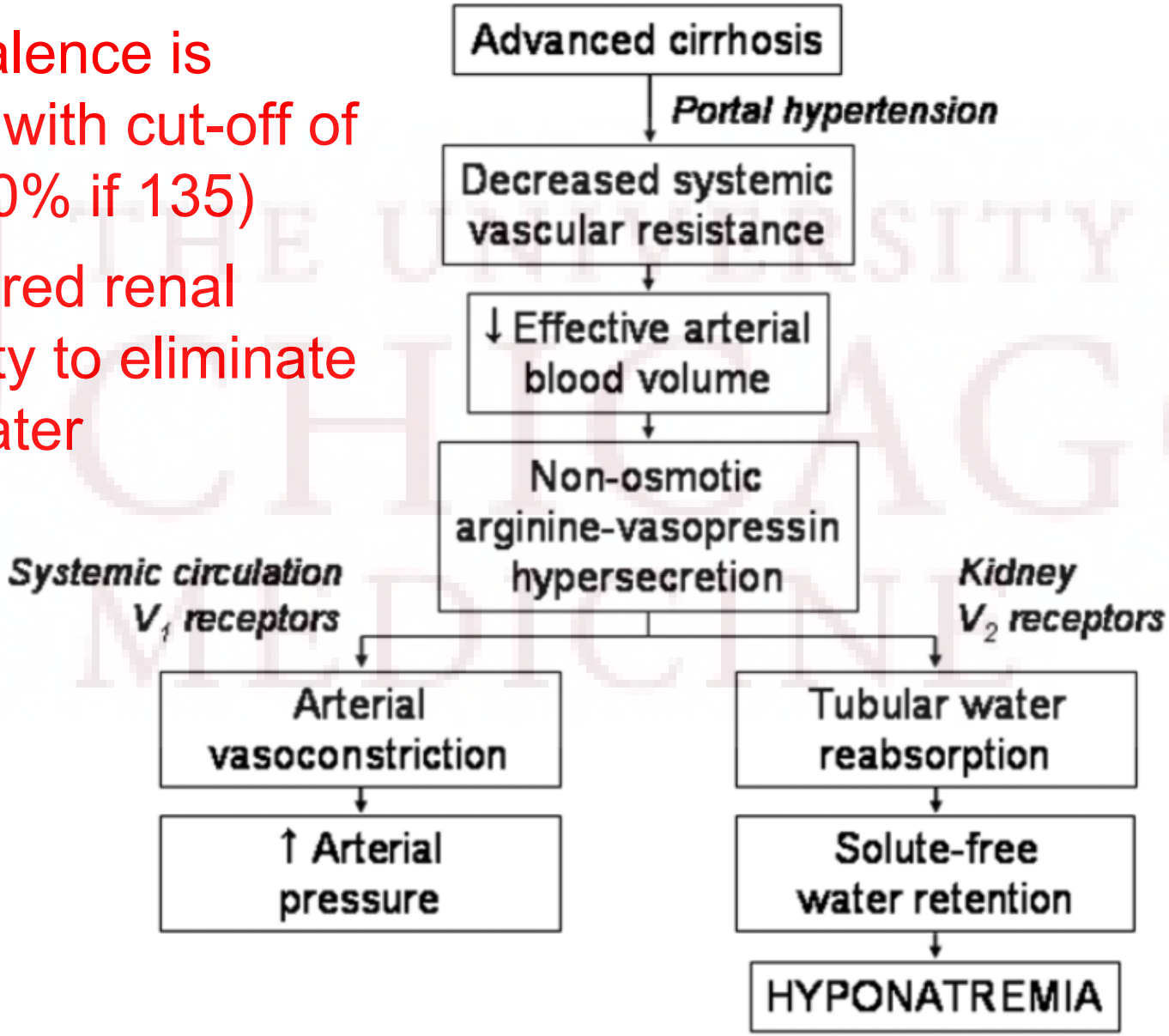
Hyponatremia in Cirrhosis

- Prevalence is 21.6% with cut-off of 130 (40% if 135)
- Impaired renal capacity to eliminate free water



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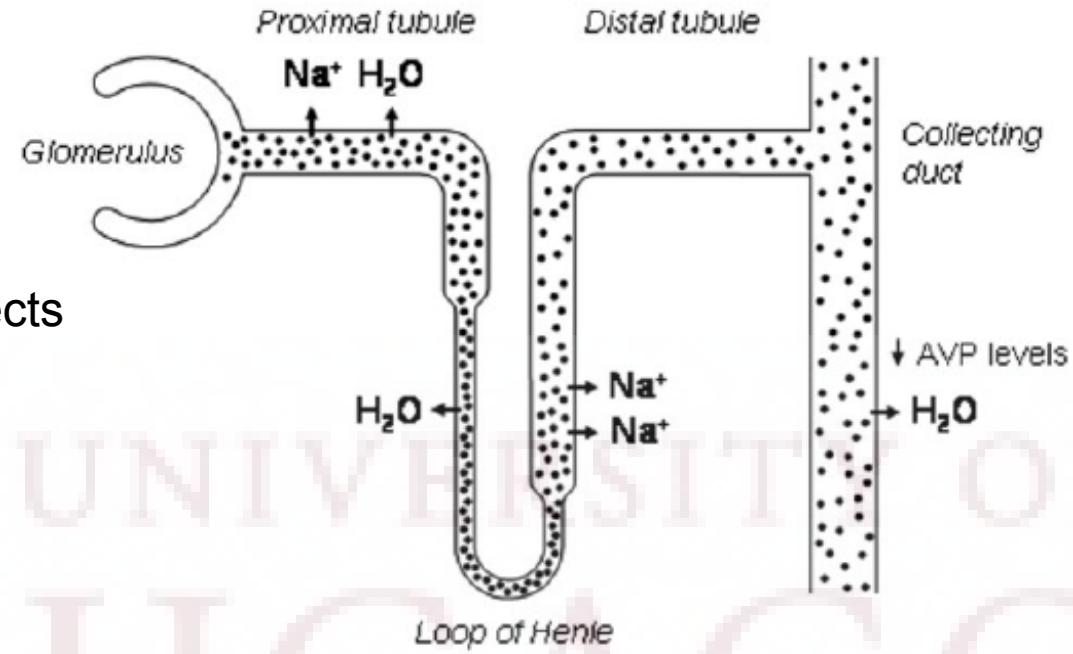
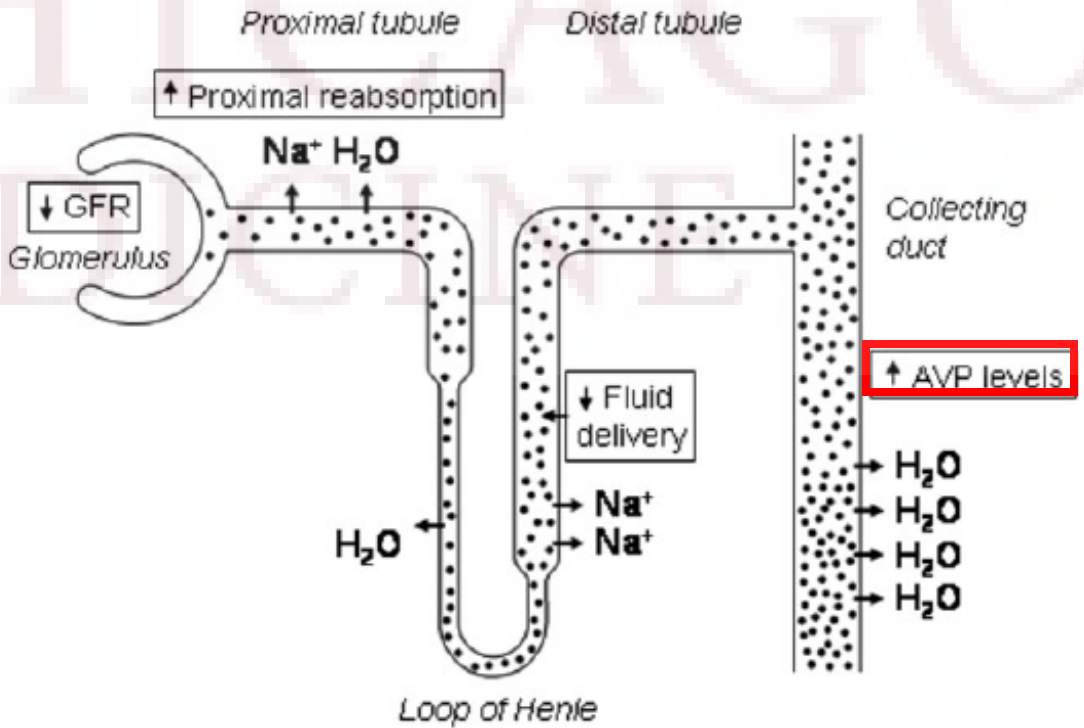
Water handling in healthy subjects



Water handling in cirrhosis



Hyponatremia in Cirrhosis

- Poor prognostic indicator
  - Risk factor for hepatic encephalopathy
  - Can be associated with renal failure
  - Patients generally have to be free water restricted
  - Worse prognosis after transplant

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Take Home Points

- AI is over-estimated in cirrhosis based on total cortisol, more standardization of free cortisol levels is needed in this population
- Effect of steroids in critically ill liver patients is still controversial
- Pathophysiology of hyponatremia in cirrhosis

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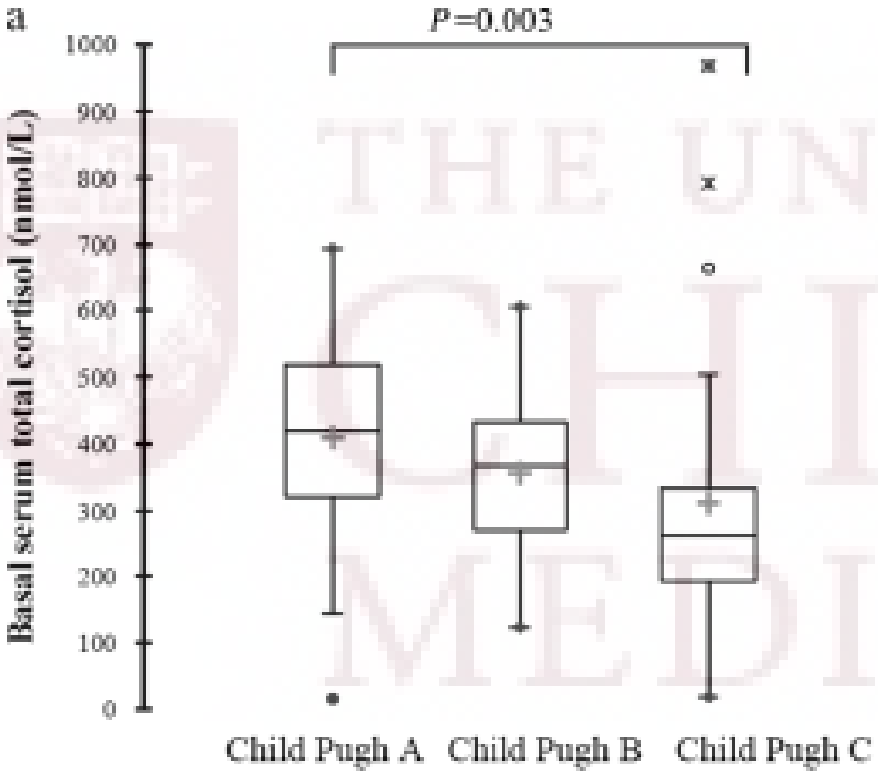

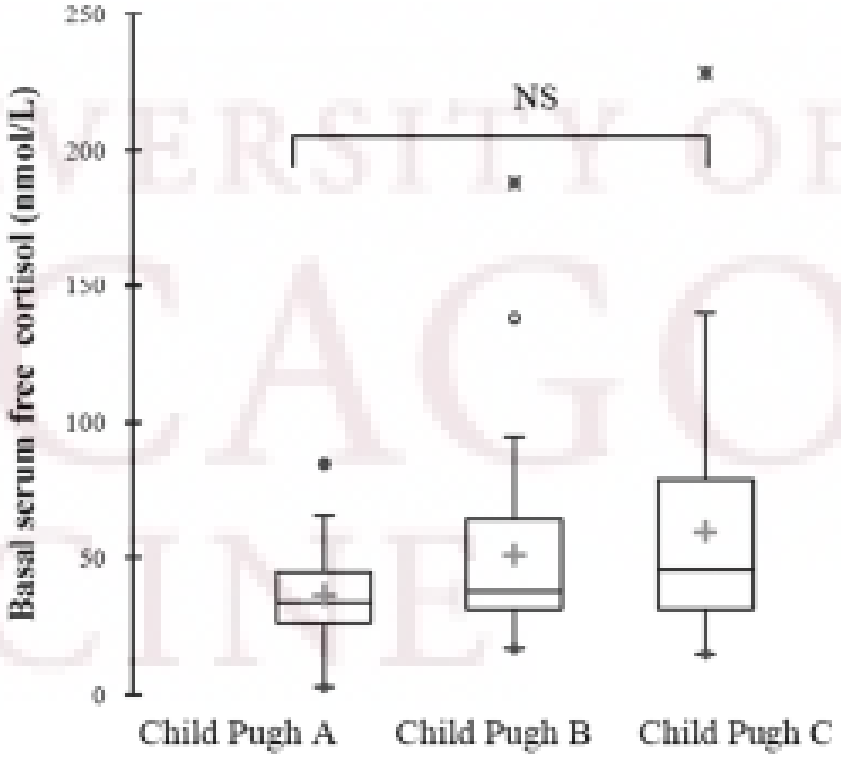

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