

Excessive amino acids in the Urine

HOSP #		WARD	A1 Paediatric Ward – Grey's Hospital
CONSULTANT	Prof. George van der Watt	DOB/AGE	27 day old Female neonate

Abnormal Result

Sodium 186mmol/L

[illegible]

Presenting Complaint

The neonate was taken to the Emergency Department due to seizures.

History

Unfortunately the attending clinician at Greys hospital did not have much of the history.

There was no history of diarrhoea according to what she remembered.

Examination

Patient was severely dehydrated clinically.

Later the patient presented with edema, signs and symptoms of nephropathy and biochemical changes in keeping with liver failure.

Laboratory Investigations

Cumulative laboratory history

Test	26/08/2020	25/08/2020	23/08/2020	18/08/2020	17/08/2020	16/08/2020	15/08/2020
Na	145	6+ 146 H	6- 141	6- 150 H	6- 164 H	6- 179 H	♦ 186 H
K	4,6	4,3	6+ 4,1	3 L	3,3 L	6- 3,8	5,2
Cl	111 H	111 H	108 H	6- 105	6- 114 H	6- 127 H	♦ 144 H
Bicarb	22 L	23	6- 22 L	6- 32 H	41 H	6+ 40 H	24
Anion gap	17 H	16	15	16	12	16	23 H
Urea	1,2 L	2	6- 2,6	10,2 H	6- 14,5 H	31,5 H	61,4 H
Creat	6- 23	6- 33	6- 45	87 H	6- 82 H	6- 126 H	198 H
Glu Random					4,4		
Lactate			2,6 H		4,4 H		
Ca	2,31		2,29		6- 2,25		2,53
Mg	0.49 L		0.47 L		6- 0.50 L		0.69 L
Phos	1,75		1,77		1,49		1,15 L
Total prot			CEGK		CEGK		49
Alb	15 L		6- 15 L		19 L		21 L
Total bili			49 H		127 H		156 H
Conj bili					103 H		
ALT			14		9		23
AST			75		53 H		89 H
ALP			6+ 211		6+ 51		36 L
GGT			140 H		140 H		128
LD			6- 467 H		726 H		952 H
CRP	27 H		13 H		6+ 24 H		6

Ferritin			CEGK		>1650		
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Table 1. Cumulative laboratory results history from newest to oldest

Urine reducing subs (screen)

Positive ++

Urine reducing substance ID (chromatography):

TLC shows the presence of trace glucose only.

Urine Amino Acid Analysis

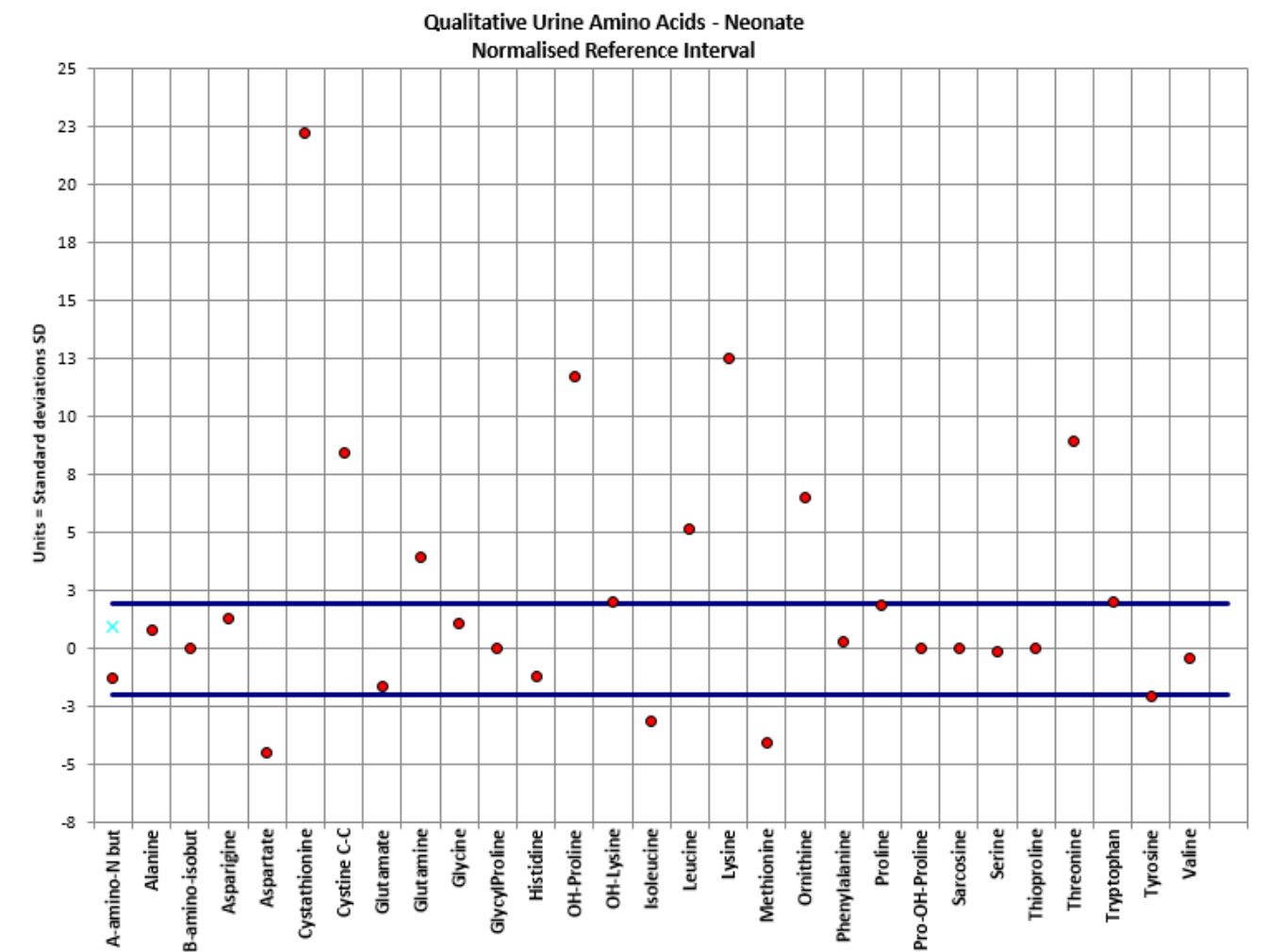


Figure 1 – Urine amino acid profile by GCMS measurement

	nmol/mg creat	Low	High		nmol/mg creat	Low	High
A-amino-N but	18	8	65	Leucine	290	78	195
Alanine	2441	982	3055	Lysine	6081	270	1850
B-amino-isobut	371	0	0	Methionine	57	342	880
Asparigine	705	185	810	Ornithine	1054	118	554
Aspartate	36	336	810	Phenylalanine	300	91	457
Cystathionine	820	16	147	Proline	2285	370	2323
Cystine C-C	1421	212	668	Pro-OH-Proline	696	0	0
Glutamate	159	70	1058	Sarcosine	1892	0	0
Glutamine	1366	393	1042	Serine	2499	1444	3661
Glycine	14131	5749	16423	Thioprolin	1	0	0
GlycylProline	159	0	0	Threonine	2318	445	1122
Histidine	1224	908	2528	Tryptophan	147	0	146
OH-Proline	1428	40	440	Tyrosine	180	220	1650
OH-Lysine	127	10	125	Valine	216	113	369
Isoleucine	49	125	390		0		

Table 2 – Urine Amino Acid results

Urine organic acids

Interpretation:

Urine organic acid analysis by GCMS demonstrates elevation of the liver markers

4-OH phenyllactate and 4-OH-phenylpyruvate together with lactaturia.

Succinylacetone, a marker for tyrosinaemia type 1 is absent. These changes

indicate underlying hepatic dysfunction with lactataemia but are non-specific

for an IMD per se. Rare forms of lactataemia include defects in pyruvate

metabolism (gluconeogenic defects such as glycogen storage disease type 1,

pyruvate dehydrogenase deficiency and thiamine deficiency). In these disorders

the lactate/pyruvate ratio is normal despite lactataemia. In pyruvate

dehydrogenase deficiency the CSF/Plasma lactate ratio is typically >2. Please

note that routine metabolic screening does not exclude galactosaemia. If

galactosaemia is suspected this should be screened for by measuring red cell

GALT activity in unspun heparin whole blood or by

screening for the common

African S135L mutation in Black South African patients. As part of our

gatekeeping policy to limit unnecessary testing, routine metabolic screening at

Red Cross Children's Hospital consists only of urine organic and amino acid

analysis. Additional tests must be requested separately based on the working

differential diagnosis and routine screening results.

Relevant legible clinical

information also aids significantly in interpreting metabolic profiles.

Other Investigations

Urine dipstick:

Blood 3+

Protein: Trace

Glucose (by glucose oxidase) ++/+++ 28 – 55 mmol/L (hence this is most likely the predominant reducing sugar – as suggested by Prof David). This is an interesting finding since the random glucose in the ward the same day was 4.4 mmol/L. Hence two possible theories: likely either severe tubular injury or, when the child had convulsions they gave a dextrose infusion which increased the plasma glucose above the renal threshold.

pH >8.5

Nitrites: Not present

Leucocytes: Not present

Urobilirubin: Trace

Bilirubin: Not present

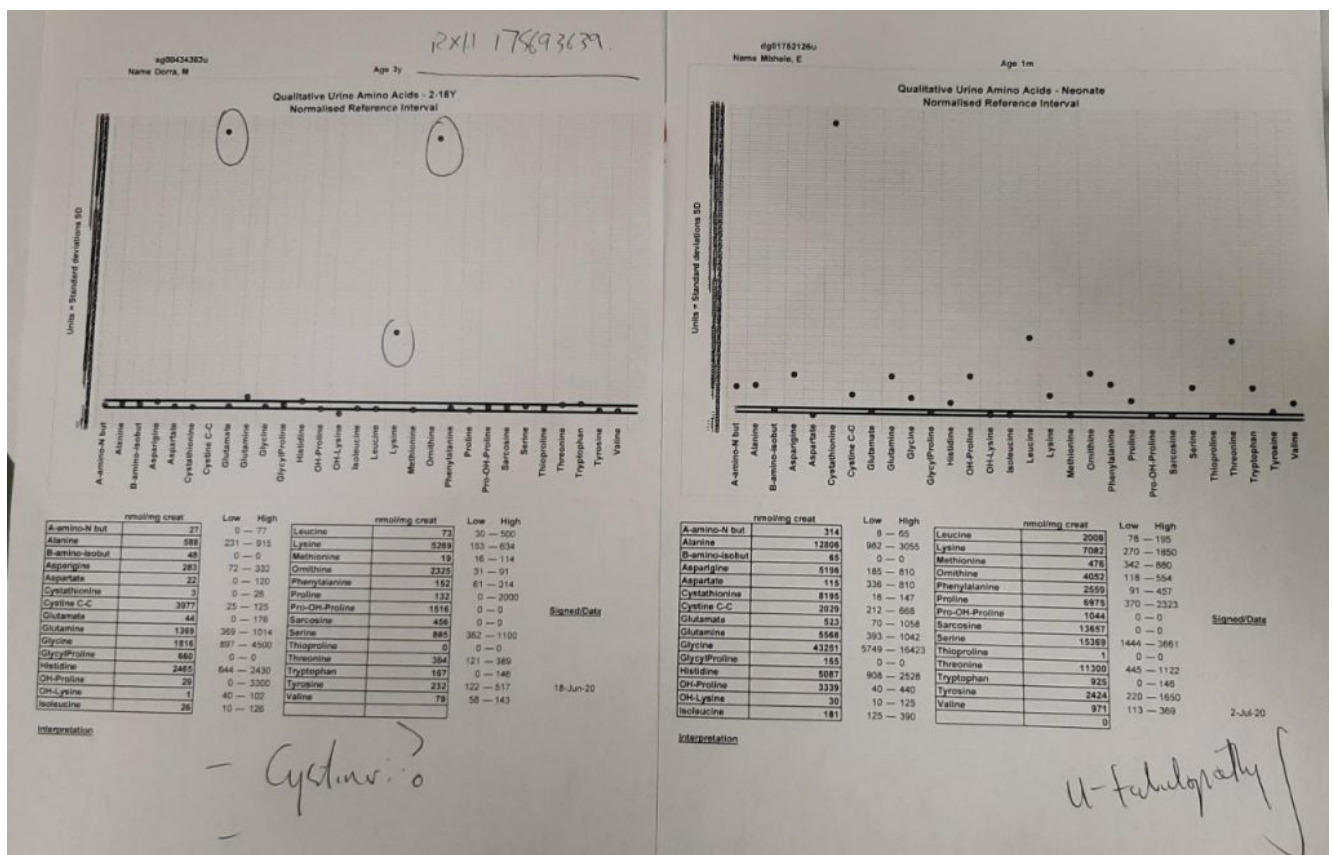
Final Diagnosis

Severe dehydration with acute kidney injury (pre-renal origin) is the most likely cause of the presentation of seizures.

Take Home Message

Dehydration is a common cause of pre-renal acute kidney injury

My thoughts initially, was that the urine amino acid screening by GCMS demonstrated a heavy generalized aminoaciduria indicative of renal tubulopathy and that cystinosis should be considered as this is the most common inheritable cause of renal tubulopathy in South Africa. However, this was later decided to be changed to rather and “evolving tubulopathy” clinical picture, as shown in the two examples below.



Typical Urine Amino acid profiles of a patient with confirmed cystinuria (left) and a patient with tubulopathy (right)

Fanconi syndrome – Generalized proximal tubular dysfunction, referred to as Fanconi syndrome, is characterized by **phosphaturia**, renal **glucosuria** (glucosuria with a normal plasma glucose concentration), **aminoaciduria**, **tubular proteinuria**, and **proximal RTA**.

The etiology of Fanconi syndrome includes inherited diseases or acquired causes [Source: [Up-to-date](#)]:

Genetic conditions associated with Fanconi syndrome include the following:

- Dent disease (X-linked recessive nephrolithiasis)
- Cystinosis
- Tyrosinemia type 1
- Galactosemia
- Wilson disease
- Lowe oculocerebrorenal syndrome, also referred to as Lowe syndrome
- Hereditary fructose intolerance
- Mitochondrial myopathies

Acquired causes of Fanconi syndrome include:

- Drugs – Medication associated with Fanconi syndrome include
 - aminoglycosides
 - cisplatin
 - ifosfamide
 - valproic acid
 - deferasirox
- Heavy metals
 - lead
 - mercury
 - cadmium

The fact that the urine dipstick was positive for glucose, suggests that either the acute kidney injury is the source of glucosuria or the patient was treated with high dose dextrose, causing the plasma glucose to overwhelm the tubular threshold for glucose transport.