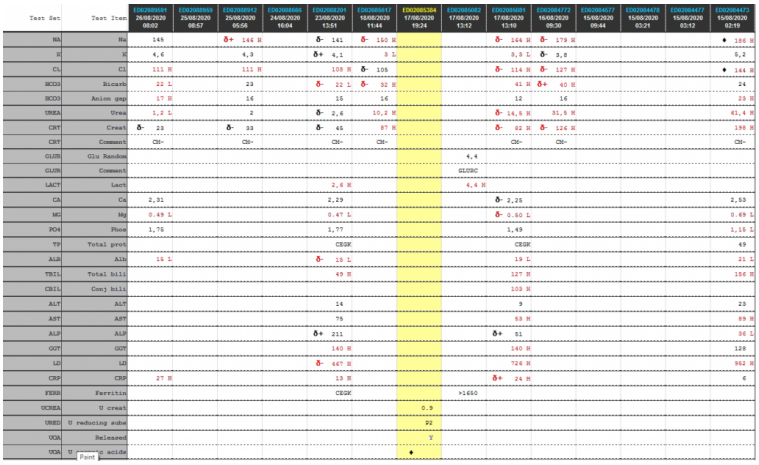
Excessive amino acids in the Urine

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



Test Set	Test Item	26/08/2020 08:02	25/08/2020 00:57	25/08/2020 05:56	24/08/2020 16:04	23/08/2020 13:51	18/08/2020 11:44	17/08/2020 19:24	17/08/2020 13:12	17/08/2020 13:19	16/08/2020 09:30	15/08/2020 09:44	15/08/2020 03:21	15/08/2020 03:12	15/08/2020 02:19
NA	Na	149	δ+ 144 H		δ- 141	δ- 150 H				δ- 144 H	δ- 179 H				♦ 186 H
K	K	4,6	4,3		δ+ 4,1	3 L				3,3 L	δ- 3,8				5,2
CL	Cl	111 H	111 H		108 H	δ- 105				δ- 114 H	δ- 127 H				♦ 144 H
HCO3	Ricark	22 L	23		δ- 22 L	δ- 32 H				41 H	δ+ 40 H				24
HCO3	Anion gap	17 H	14		15	16				12	16				23 H
UREA	Urea	1,2 L	2		δ- 2,6	10,2 H				δ- 14,5 H	31,5 H				61,4 H
CRT	Creat	δ- 23	δ- 33		δ- 45	87 H				δ- 82 H	δ- 126 H				198 H
CRT	Comment	CH-	CH-		CH-	CH-				CH-	CH-				CH-
GLUS	Glu Random								4,4						
GLUS	Comment								GLUSC						
LACT	Lact				2,6 H				4,4 H						
CA	Ca	2,31			2,29					δ- 2,25					2,53
MG	Mg	0.49 L			0.47 L					δ- 0.50 L					0.69 L
PO4	Phos	1,76			1,77					1,49					1,15 L
TP	Total prot				CEGK					CEGK					49
ALB	Alb	16 L			δ- 15 L					19 L					21 L
TBIL	Total bili				49 H					127 H					186 H
CBIL	Conj bili									103 H					
ALT	ALT				14					9					23
AST	AST				75					63 H					89 H
ALP	ALP				δ+ 211					δ+ 51					96 L
GGT	GGT				140 H					140 H					129
LD	LD				δ- 467 H					724 H					962 H
CRP	CRP	27 H			13 H					δ+ 24 H					6
FERR	Ferritin				CEGK				>1650						
UCREA	U creat							0.9							
URED	U reducing subs							99							
UOA	Released							Y							
UOA	U amino acids							♦							

Paed

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

Ferritin			CEGK		>1650		

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

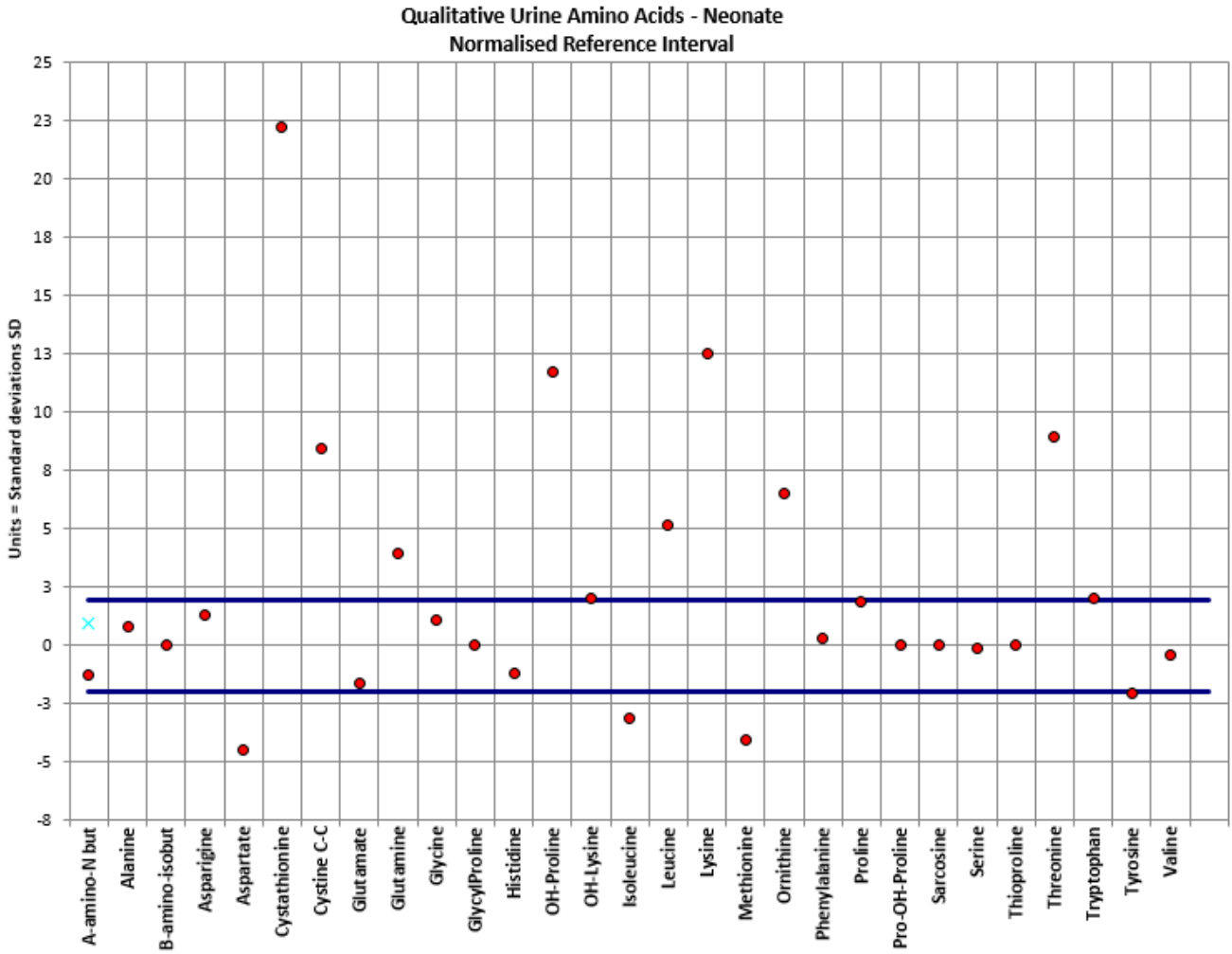


Figure 1 – Urine amino acid profile by GCMS measurement

	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	Thioproline	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

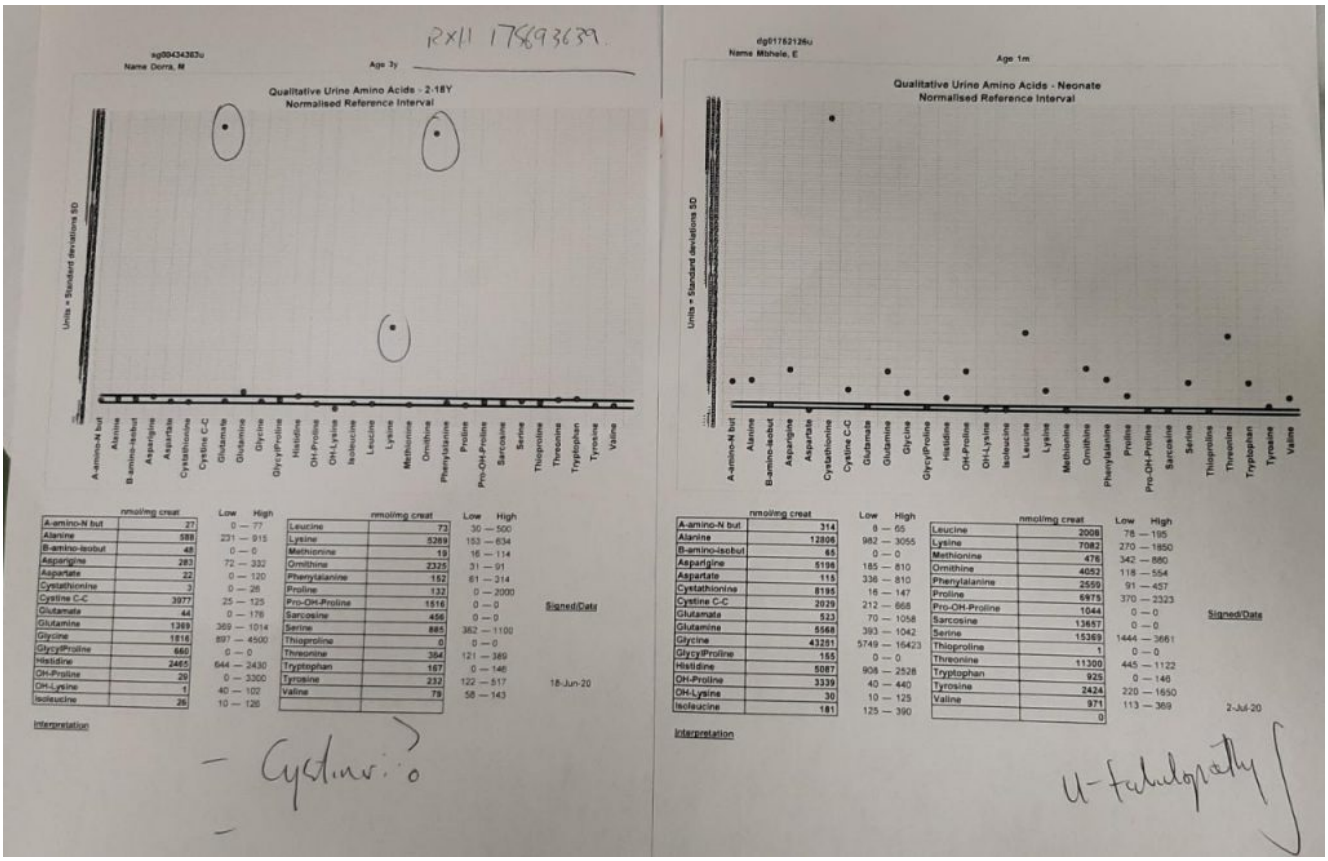
Final Diagnosis

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.