

Clinical Characteristics

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Age of onset:

Biochemical abnormalities

- diagnosis as adult does not exclude earlier presence of biochemical abnormalities
- seen as early as (premature) neonates
Tammaro et al, *Pediatr Nephrol.* 2010 Oct;25(10):2179-82
- Normal biochemistries aged 2 years in affected patient documented
Riveira-Munoz, *JASN* 18:1271-1283
- Hypomagnesaemia may develop later than hypokalaemic alkalosis
Tammaro et al, *Pediatr Nephrol.* 2010 Oct;25(10):2179-82

Tammaro et al

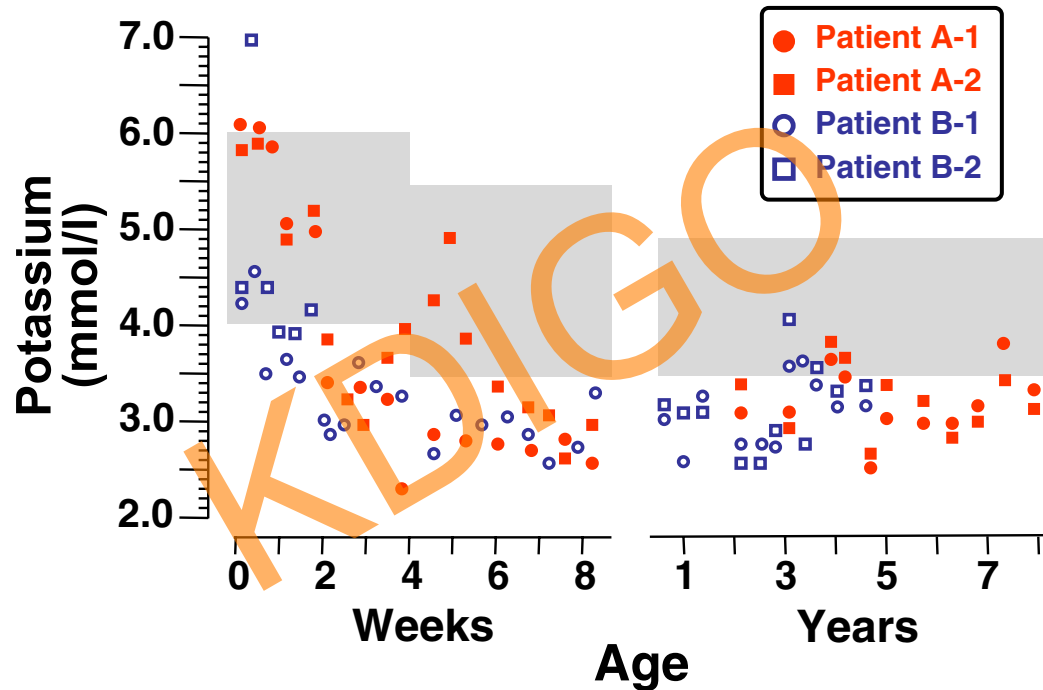


Fig. 1 Plasma potassium levels in two pairs of prematurely born twins (*A-1/A-2* and *B-1/B-2*, respectively) with Gitelman syndrome. *Shaded frame* Reference values

Age of onset: symptoms

- As most patients present school age or later: symptoms typically develop that age?
- Youngest age with reported symptoms: 5 months: ventricular arrhythmia
- Other reports: around 2 years of age: growth delay, hypotonia, dysesthesia, abdominal pain

Cortesi et al, *Nephrol Dial Transplant* 2005; **20**: 1981-1983

Riveira-Munoz, *JASN* 18:1271-1283 , Vargas-Poussou *JASN* 22:693-703

Spectrum of symptoms: children

- Most common in German and Belgian cohort: carpopedal spasm and growth delay
Peters et al: American journal of medicine 112:183-190.
Vargas-Poussou JASN 22:693-703
- In Spanish cohort: 71% report symptoms, such as muscle cramps, asthenia, muscle weakness and myalgias.
Herrero-Morin, NDT 26:151-155
- Of these, 88% stated that symptoms did not interfere with mood or social relationship
- Rhabdomyolysis, cardiac arrhythmia: rare and not always with genetic confirmation
von Vigier, Pediatric nephrology 25:861-866
Zanolari et al :Nephron 91:762-763

Spectrum of symptoms: adults

- American cohort: 80% reporting fatigue, dizziness, cramps and score lower than controls on QOL
Cruz et al: Kidney international 59:710-717 .
- Italian cohort: 17% report their symptoms as “debilitating”
Caiata-Zufferey, NDT 27:3196-3201.
- Other reported symptoms: arthralgia, polyuria/polydipsia, enuresis, constipation, vomiting, paresthesias, palpitations, paralysis

Paediatric specific symptoms

Growth retardation:

- Growth delay (often with pubertal delay) is recurrently reported
- In one cohort, 3/25 patients are reported to have “final short stature” (<3rd %ile)

Riveira-Munoz, JASN 18:1271-1283

Adult specific symptoms

Chondrocalcinosis:

- Ca Pyrophosphate crystal deposition in joints and/or sclerae
- ?related to hypomagnesaemia
- Dx by biopsy or radiography
- Can lead to arthropathy mimicking gout, ankylosing spondylitis/crowned dens syndrome

Adult specific symptoms

- Debilitating illness?
- Polyuria/polydipsia?

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Variability: Biochemical abnormalities

value	Vargas-Poussou JASN 22:693-703 range	Peters et al: American journal of medicine 112:183-190 2SD	Riveira-Munoz, JASN 18:1271-1283 ?	Herrero-Morin, NDT 26:151-155 ?
K [mmol/l]	1.3-3.5	2.3-3.1	2.2-2.7	2.3-3.2
Cl [mmol/l]	91-102	?	?	?
TCO2 [mmol/l]	24-33	?	30.6-32.5	25.3-31.1
Mg [mmol/l]	0.34-0.84	0.35-0.75	0.44-0.56	0.42-0.64
Urine osm [mosmol/kg]	?	600-900	?	?
Urine Ca	0.01-0.29 (Ca/ Crea ?unit)	0-3 mg/kg/d	0.028-0.086 Ca/Crea mg/mg	0-0.07 Ca/Crea mg/mg

Inter-individual variability of symptoms

Table 3. Prevalence of symptoms in Gitelman's syndrome

	Gitelman's syndrome	Controls	<i>P</i>
	%		
General			
Fatigue	82	68	0.172
Dizziness	80	40	0.0005
Fainting	34	0	0.0009
Musculoskeletal			
Generalized weakness	44.2	0	<0.00001
Muscle weakness	70	4	<0.00001
Cramps	84	40	0.0001
Carpopedal spasm/tetany ^a	11.7	NA	NA
Muscle stiffness or pain	52	28	0.048
Paralysis ^a	6	NA	NA
Arthralgia	54	36	0.141
Renal			
Nocturia	80	24	<0.00001
Polydipsia	64.6	36	0.066
Polyuria	50	16	0.004
Thirst	76	12	<0.00001
Enuresis	11.9	4	0.273
Salt craving	90 ^b	20	<0.00001
Hypotension	62	12	0.00004
Gastrointestinal ^c			
Vomiting	8	NA	NA
Constipation	16	NA	NA
Abdominal pain	16	NA	NA
Paresthesias	78	20	<0.00001
Palpitations	62	24	0.002

NA is not applicable.

^a As indicated by referring physician (**Methods** section)

^b Noted as an adult 90%; noted as a child 87.8%

^c Patients were asked if they experienced these symptoms when they had low potassium and/or magnesium levels, therefore not applicable to controls

Intra-individual variability of symptoms

- Symptoms may worsen with menses

Cruz et al: Kidney international 59:710-717

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Perception of symptoms

Patients categorised as:

- Disabling illness
- Normalised illness
- Different normality
- Episodic disability

Caiata-Zufferey et al. NDT, 27:3196-3201

Summary

- Wide range in age of onset of symptoms/
diagnosis
- Wide range in (?perceived) severity of illness
- ?ascertainment bias (only symptomatic
patients are diagnosed)