Pediatric polyuria polydipsia

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Polyuria

Adults urine output > 3 L/day

Children >2 L/m2, or 50 mL/kg /24 h

Polydipsia

> 3 liters in 24 hours

Differential diagnosis of Polyuria

Solute diuresis	
Glucosuria	Hyperglycemia, SGLT2 inhibitor use
Urea	Azotemia, Tx, tissue catabolism
Sodium	IV volume expansion, post obstruction
Mannitol	For ↑ICP

urine osmolarity o>600 mosm/kg

Water diuresis	
Primary polydipsia	
Central diabetes insipidus	
Nephrogenic diabetes insipidus	

urine osmolarity <600mosmol/kg

Diagnostic Approach

- **History & Clinical Examination**
- Presence of neurological symptoms
- **Laboratory Evaluation**
  - **Serum & Urine Osmolality**
  - **Plasma Sodium & Electrolytes**
  - **Glucose & HbA1c**
  - **Calcium & Potassium**
  - **Vasopressin (AVP) Levels**
  - Copeptin levels if available

Diagnostic Approach

-Water Deprivation Test & Desmopressin Challenge:

	Water deprivation test	Desmopressin
Primary Polydipsia	Gradual increase in urine osmolality	no response
Central DI	No increase in urine osmolality	significant response (>50% increase)
Nephrogenic DI	No increase in urine osmolality	No increase in urine osmolality

- **MRI Brain**
- **Genetic Testing**

Huynh T et al. Paediatric perspectives in the diagnosis of polyuria-polydipsia syndrome. Clin Endocrinol (Oxf). 2024 Dec;101(6):580-592.

Copeptin as a Diagnostic Biomarker
an alternative to water deprivation test

The C-terminal peptide of pro-vasopressin and is co secreted with ADH from the posterior pituitary

The plasma levels of copeptin strongly correlate with plasma ADH

commercially available blood assay

1. Stable and easier to measure

2. Baseline Copeptin (without stimulation):
   - <2.5 pmol/L suggests Central Diabetes Insipidus
   - 21.4 pmol/L strongly suggests Nephrogenic Diabetes Insipidus

3. Hypertonic Saline-Stimulated Copeptin:
   Primary polydipsia vs Diabetes Insipidus
   A low stimulated copeptin → Central Diabetes Insipidus

Congenital NDI Clinical Presentation

-normal birth weight
-pregnancies are not complicated by polyhydramnios.
-The urine-concentrating defect is present from birth
-With breast milk feedings, infants usually thrive and do not develop signs of dehydration.
With cows' milk formula feedings, the osmole load to the kidney increases, resulting in an increased demand for free water hypernatremic dehydration

Symptomes-

Polyuria and polydipsia, irritability, poor feeding, recurrent vomiting, poor weight gain
Rare: Seizures, mainly during therapy, particularly if rehydration proceeds too rapidly.
Children-Constipation, Nocturia and nocturnal enuresis

NDI in Soroka medical center

20 patients<18yo

AQP2 mutation
Mean age on diagnosis
6 weeks
~50% w/ **AQP2 mutation** c.83 T>C
patients w/ undiagnosed siblings

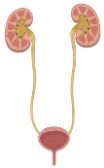
V2R mutation
4 male patients

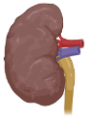
AQP2 presentation parameters
Symptomes: Hypernatremia - 27 (81.8%)
Fever – 20 (60.6%)
Weight loss – 12 (36.4%)
Sepsis work up – 10 (30.3%)
Labs-B osm 330 U osm 119
B Na 162 U Na

Mortality 2

Long term outcome

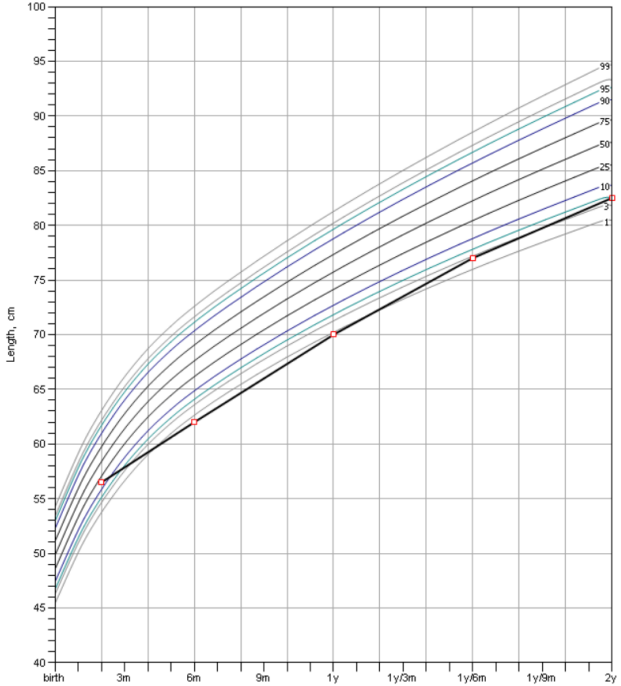
Urologic complications
40.6% in AQP2
Hydroureteronephrosis
Large capacity bladder
Trabeculated bladder
CIC6
0 % in V2R

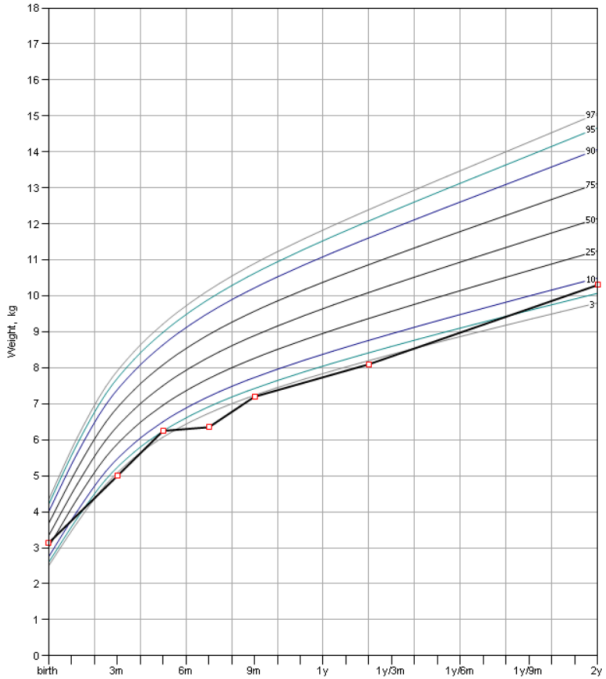




kidney function
In AQP2 Adults median eGFR 110 ml/min/1.73m²
Current B Na 141 B osmol 283
4 patients developed CKD
3 on Dialysis
In V2R no adults

Growth in our patients





Compromised growth Age< 2 years, below 3rd percentile

נערך ע"י ד"ר אודיה דויד
אנדוקרינולוגיה אסותא
אשדוד

Growth in NDI

30 patients

Untreated patients fail to grow normally

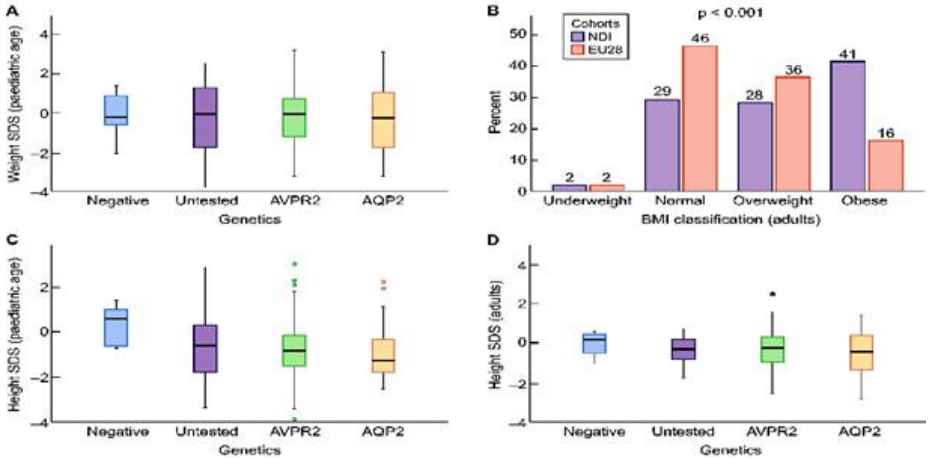
Untreated : Growth< 50th percentile, SD<1

Welltreated:

normal adult height

Catch-up growth

Bone maturation is generally not delayed



-van Lieburg AF, Knoers NVAM et al. Clinical presentation and follow-up of thirty patients with congenital nephrogenic diabetes insipidus. J Am Soc Nephrol. 1999;10:1958–64.

-Lopez-Garcia SC et al. European NDI Consortium; Bockenhauer D. Treatment and long-term outcome in primary nephrogenic diabetes insipidus. Nephrol Dial Transplant. 2020 Dec 26.

Q&A

Long term outcome

Growth?
Kidney function?
Urological complications?
Discontinue drugs in adolescence/adults?

Treatment and future options

- In symptomatic infants and children, we recommend starting treatment with a **thiazide and prostaglandin synthesis inhibitors**
- We recommend adding **amiloride** to thiazide in patients with hypokalaemia induced by thiazides

- **Drug repurposing** metformin, sildenafil, simvastatin, clopidogrel
- **Restore the accuracy of protein folding** in mutations that do not lead to a complete loss of function.
- **Ggene mutation/ gene therapy**

Levtchenko, E. *et al.* International expert consensus statement on the diagnosis and management of congenital nephrogenic diabetes insipidus (arginine vasopressin resistance). *Nat Rev Nephrol* **21**, 83–96 (2025).

Duicu C. et al.NDI in children 2021

Thank you