

TYPE 4 RTA IN DIABETES MELLITUS

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INTRODUCTION

- **Diabetes mellitus**—especially long-standing type 1 or type 2—can cause:

Hyporeninemic hypoaldosteronism

- ↓ Renin → ↓ Aldosterone → impaired potassium & hydrogen ion excretion.
- **Autonomic neuropathy** → ↓ renin release.
- Diabetic nephropathy → **affects juxtaglomerular apparatus** → ↓ renin-angiotensin-aldosterone system (RAAS) activation.



RENAL TUBULAR ACIDOSIS

NONGAP METABOLIC ACIDOSIS WITH HYPERCHLOREMIA

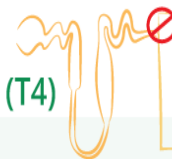
DISTAL RTA (T1)

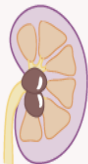


PROXIMAL RTA (T2)



HYPERKALEMIC RTA (T4)



DEFECT	DECREASED DISTAL H^+ SECRETION. ➔ No new HCO_3^- is generated.	DECREASED PROXIMAL HCO_3^- REABSORPTION.	ALDOSTERONE DEFICIENCY/RESISTANCE ➔ Hyperkalemia, Reduced NH_4^+ excretion
CAUSES	Amphotericin B tox., Analgesic nephropathy Autoimmune disease (SLE, Sjögren's) Urinary tract obst.	Fanconi syndrome Carbonic anhydrase inhbs. Multiple myeloma	Diabetic or obstructive nephropathy, Chronic interstitial nephritis, Adrenal insufficiency. ACE inhbs/ARBs, K^+ -sparing diuretics, TMP-SMX
S/Sx	Polydipsia, polyuria. Muscle weakness Nephrolithiasis (hypercalciuria, hypocitraturia) Growth retardation, Rickets 	Muscle weakness Growth retardation, Rickets 	Poss. muscle weakness, cardiac arrhythmias (if hyperkalemia is severe) 
URINE PH	> 5.5	> 7 IF PLASMA HCO_3^- IS NORMAL < 5.5 IF PLASMA HCO_3^- IS DEPLETED	< 5.5
SERUM HCO_3^- & K^+	HCO_3^- = 10-15 mmol/L K^+ ↓	HCO_3^- = 16-20 mmol/L K^+ ↓	HCO_3^- = > 17 mmol/L K^+ ↑
DIAGNOSIS	NH_4^+ loading test -> positive urinary anion gap.	HCO_3^- loading test -> FE HCO_3^- > 15%, urine pH > 7.5	Urinary K^+ < 40 mmol/L or FE K^+ < 20% Abnormal serum aldosterone
TREATMENT	Sodium HCO_3^- or Potassium citrate Thiazide diuretics	Sodium HCO_3^- or Potassium citrate Thiazide diuretics	Volume expansion, dietary K^+ restriction K^+ -wasting diuretics

Typical biochemical features

TYPE 4 RTA

Parameter

Serum K⁺

Serum HCO₃⁻

Anion gap

Urine pH

Urinary ammonium excretion

**Trans tubular potassium gradient
(TTKG)**

Finding

↑ (hyperkalemia)

↓ (mild metabolic acidosis, usually
15–20 mmol/L)

Normal (non-anion gap metabolic
acidosis)

< 5.5 (kidneys can acidify urine, unlike
type 1 RTA)

Low (despite acidosis)

Low (inappropriately low in
hyperkalemia)

TTKG- TRANSTUBULAR POTASSIUM GRADIENT

- **Formula for TTKG**
- **TTKG** =
$$\frac{\text{Urine K}^+ \times \text{Plasma osmolality}}{\text{Plasma K}^+ \times \text{Urine osmolality}}$$
- **Urine K⁺** = urinary potassium concentration (mmol/L).
- **Plasma K⁺** = plasma potassium concentration (mmol/L).
- **Urine osmolality** = urine osmolality (mOsm/kg).
- **Plasma osmolality** = plasma osmolality (mOsm/kg).

TTKG INTERPRETATION

- **Normal TTKG values :**
- **In hyperkalemia:** TTKG should be **>7–10** → indicates appropriate renal K^+ excretion.
- **In hypokalemia:** TTKG should be **<3** → indicates appropriate renal K^+ conservation.

- **In Type 4 RTA, despite hyperkalemia:**
- The **TTKG is low (<7)**, showing impaired K^+ secretion.
- This suggests either:
 - Low aldosterone levels (hypoaldosteronism).
 - Aldosterone resistance (tubular dysfunction).

TREATMENT

- **Dietary** potassium restriction.
- **Loop or thiazide diuretics** (enhance K^+ excretion).
- **Fludrocortisone** (mineralocorticoid replacement, if no contraindications like hypertension or fluid overload).
- **Sodium bicarbonate** to correct acidosis.