

SERUM VITAMIN D LEVELS AND EXPRESSION OF VITAMIN D RECEPTOR (VDR) IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD).

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Introduction

- The progression of Autosomal Dominant Polycystic Kidney Disease (ADPKD) is associated with kidney enlargement due to cyst growth and activation of the Renin-Angiotensin-Aldosterone system (RAAS), which may lead to hypertension and cell proliferation. Hypertension in its turn, is associated to a further increase in kidney volume and progression of ADPKD.
- The active form of vitamin D [1,25(OH)₂D₃] is known as a suppressor of renin gene transcription by a Vitamin D receptor (VDR) mediated mechanism.
- Observational studies in the general population have shown that serum levels of vitamin D [25(OH)D] are negatively associated with arterial blood pressure.

Aims

- The aim of the present study was to assess vitamin D status and expression of vitamin D receptor (VDR) and the association with kidney volume and hypertension in ADPKD patients.

Subjects

- 74 patients (44F/30M, 40 ± 12 years old) with ADPKD based on family history and diagnosed according to ultrasonographic criteria by Pei et al (JASN 2009)

Methods

- **Serum biochemistry and hormonal determinations**
- **Vitamin D Receptor (VDR) expression:**
 - VDR expression in peripheral monocytes retrieved from blood samples was determined by flow cytometry
- **Total Kidney Volume/height (TKV/h):**
 - Assessed by Magnetic Resonance Imaging (MRI) and corrected for height (ht)
- **Hypertension:**
 - Hypertension was considered on the basis of a history of hypertension, present blood pressure measurements, or actual/past use of antihypertensive medications.
- **Hypovitaminosis D**
 - Serum 25 (OH) D levels below 30 ng/ml was considered as hypovitaminosis D, according to K-DOQI guidelines.

Results

Table 1: Total Kidney Volume (TKV) and serum parameters according to serum levels of vitamin D.

Parameters	25(OH)D (ng/mL)	
	≥ 30 (n=22)	< 30 (n=52)
25(OH)D (ng/ml)	37 ± 7	21 ± 5*
1,25 (OH) ₂ D ₃ (pg/ml)	18 ± 8	22 ± 8*
VDR (MFI)	1461 ± 1122	1108 ± 893
Renin (ng/ml.h)	8.6 (0.10-60)	7.3 (0.20-60)
Aldosterone (ng/dl)	11.2 (0.90-23.70)	8.0 (0.90-39)
PTH (pg/ml)	54 ± 51	74 ± 75*
FGF-23 (pg/ml)	333 (53-4527)	162 (55-7280)
Alkaline phosphatase (UI/L)	58 ± 12	60 ± 19
Total Kidney volume (mL)	932 (545- 1388)	1257 (725- 1821)
Total Kidney Volume/ht (mL)	552 (308- 818)	782 (440- 1054)

X SD; # Median (25th to 75th percentile); * p<0.05; MFI: Median Fluorescence Intensity.

Table 2. Correlation (r) between parameters.

Parameters	25(OH)D (ng/mL)	1,25(OH) ₂ D ₃ (pg/ml)	VDR (MFI)
Systolic BP (mmHg)	r = 0.01	r = -0.06	r = -0.10
Diastolic BP (mmHg)	r = 0.06	r = 0.00	r = -0.26
Plasma renin (ng/ml.h)	r = -0.06	r = -0.05	r = -0.28#
Serum aldosterone (ng/dl)	r = -0.03	r = 0.09	r = 0.03
Total Kidney Volume TKV (ml)	r = -0.36*	r = 0.05	r = -0.22
Total Kidney Volume TKV/ht (mL)	r = -0.33*	r = 0.12	r = 0.13
Creatinine Clearance (ml/min/24h/1,73 m ²)	r = 0.02	r = 0.16	r = 0.17

BP: Blood Pressure; MFI: Median Fluorescence Intensity. *p≤ 0.006, #p≤ 0.04

Summary

- Seventy-three (73) % of patients were hypertensive, 44.5 % were CKD stage 1, 30.5% CKD stage 2, 25% stage 3 to 5.
- Forty-two (52) out of 74 (70.5%) presented insufficient levels of 25(OH)D (< 30 ng/mL).
- There has been no statistical differences between vitamin D sufficient or insufficient patients with respect to renal function, presence of microalbuminuria, FGF-23, Alkaline Phosphatase, Aldosterone and Plasma Renin and percentage of hypertension (77 vs 71%, respectively).
- The mean TKV/h was higher in vitamin D-insufficient patients but it did not reach statistical significance (1377 ± 966 vs 1042 ± 730 mL). However, a significant and inverse correlation was found between serum vitamin D levels and TKV (r= -0.36, p < 0.01), TKV/ht (r= -0.33, p= 0.005) and between VDR expression and Plasma Renin (r= -0.28, p < 0.05)

Conclusion

- The present findings indicate that lower levels of vitamin D were associated with larger kidneys in this population of ADPKD patients and the inverse association between expression of VDR and plasma renin further suggested an upregulation of renin in the kidney.
- The high percentage of hypertensive patients under treatment might have been responsible for the absence of association between blood pressure and vitamin D.

