DOI: 10.7860/JCDR/2021/49065.15212

Original Article

Internal Medicine Section

The Relationship of Vitamin D Level with Renal Prognosis in Focal Segmental Glomerulosclerosis Patients- A Retrospective Study

CAGDAS KUCUKERDOGAN[1], EBRU GOK OGUZ[2], GULAY ULUSAL OKYAY[3], HATICE SAHIN[4], TAMER SELEN[5], MEHMET DENIZ AYLI[6]

ABSTRACT

Introduction: The level of 25-hydroxyvitamin D_3 is an independent predictor of disease progression and death in Chronic Kidney Disease (CKD) patients. However, there are insufficient data to evaluate the possible effects of plasma 25(OH)D_3 levels on the prognosis of Focal Segmental Glomerulosclerosis (FSGS).

Aim: To analyse the relationship between renal prognosis and serum 25(OH)D_3 status in FSGS.

Materials and Methods: The study was conducted on 56 patients, who were followed-up for at least one year and diagnosed with primary FSGS. Participants were grouped according to their baseline 25(OH)D_3 levels (≤15 or >15 ng/mL) and treatment response at the end of one year (remission group or no remission group) was evaluated.

Results: Mean age of the 56 participants was 44±13.92 years and 27 (48.2%) were male. Remission achievement in the first year was significantly higher and interstitial fibrosis was significantly lower for the group with a 25(OH)D_3 above >15 ng/ mL (p<0.001, p=0.002, respectively). Basal serum 25(OH)D_3 level was significantly lower and interstitial fibrosis and tubular atrophy percentages were higher for the 'no remission' group (p<0.001, p<0.001, p=0.005, respectively). Results of the binary logistic regression analysis revealed that low 25(OH)D_3 level and higher interstitial fibrosis were independent predictive factors that increased the risk of no remission in the first year (p=0.036, p=0.004, respectively).

Conclusion: In primary FSGS patients, low baseline 25(OH)D_3 level at the time of biopsy and high interstitial fibrosis are independent predictors that reduce remission rates in the first year.

Keywords: 25-hydroxyvitamin D_3, Interstitial fibrosis, Remission

INTRODUCTION

Vitamin D deficiency is quite common in people with CKD [1]. It has been shown that 25(OH)D_3 concentration is associated with daily protein excretion, estimated Glomerular Filtration Rate (eGFR), and annual decline in kidney function [2,3]. Plasma levels decrease further as kidney function declines and current data suggest that 25(OH)D_3 level is an independent predictor of disease progression and death in CKD patients [4-6]. FSGS is the second most common glomerular disease after membranous glomerulonephritis in Turkey and one of the important causes of CKD [7-9]. The presence of nephrotic range proteinuria, the degree of interstitial fibrosis and response to treatment are some predictive factors for the long term prognosis of FSGS patients [10,11].

The 25 (OH) Vitamin D is an important vitamin that has critical role in the maintenance of the cardiovascular, neurological and immune systems [12]. Vitamin D replacement is extremely important in patients with stage 3-5 CKD, as it prevents secondary hyperparathyroidism [5]. Vitamin D analogues have been shown to reduce renal progression in diabetic nephropathy and glomerular damage in experimental studies [13,14]. However, there is insufficient data on whether 25(OH)D_3 deficiency is a risk factor for disease progression in FSGS patients with nephrotic syndrome. Demonstrating a possible relationship between vitamin D level and renal prognosis in FSGS, one of the most common primary glomerulonephritis, may have important consequences for this patient population at high risk of end stage renal disease. The aim of this study was to evaluate the relationship between 25(OH)D_3 levels and clinical parameters, renal histological lesions and renal prognosis in FSGS patients.

MATERIALS AND METHODS

This retrospective study was conducted between June 2006 and August 2018 at University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Nephrology Clinic, Ankara, Turkey. Analysis of the data was done in January 2021. The study was initiated after obtaining permission from the local Ethics Committee (date: 06.08.2018, number: 53/21).

Inclusion criteria: Total 56 of 80 FSGS patients diagnosed with biopsy in the clinic, who were followed for at least one year after biopsy, were included.

Exclusion criteria: Those who had biopsy less than a year ago and those who did not attend their regular follow-ups were excluded from the study.

Study Procedure

Age and gender were noted as demographic data. Arterial hypertension, Diabetes Mellitus (DM) and Cardiovascular Diseases (CVD's) were recorded as concomitant diseases. The results of serum samples were taken when the patients were admitted to the clinic for renal biopsy were evaluated as baseline laboratory tests. Interstitial fibrosis and tubular atrophy were assessed on kidney biopsy and recorded as the percentage of glomeruli examined.

Serum glucose, urea, creatinine, serum cholesterol, albumin and 25(OH)D_3 levels were noted as laboratory parameters. A 25(OH)D_3 levels studied by the chemiluminescence method were interpreted according to the National Kidney Foundation Results Quality Initiative (NKF K/DOQI) guidelines {25(OH)D_3> 30 ng/mL is normal; 16 and 30 ng/mL range is insufficient; <15 ng/mL is deficiency} [15]. Participants were primarily divided into two groups based on their baseline vitamin D status. Those with levels below 15 ng/mL

constituted group-1, while those above 15 ng/mL formed group-2. Participants were also divided into remission group and no remission group according to their treatment responses at the end of one year.

Treatments and treatment responses were based on the recommendations of the Developing Global Outcomes of Kidney Disease (KDIGO) Clinical Practice Guidelines for Glomerulonephritis. Reduction of proteinuria to 0.3-3.5 g/dL {or spot urine protein/creatinine ratio 300-3500 mg/g (0-350 mg/mmol)}, and stable serum creatinine (change in creatinine <25 %), or a decrease in proteinuria >50% from baseline and stable serum creatinine (change in creatinine <25%) were used to define partial remission of nephrotic syndrome in adults with FSGS. On the other hand, reduction of proteinuria to <0.3 g/day, or spot urine protein/creatinine ratio <300 mg/gr (<30 mg/mmol), and normal serum creatinine and serum albumin >3.5 g/dL (35 g/L) were used as parameters to define complete remission [16].

STATISTICAL ANALYSIS

Data were analysed using Statistics Package for Social Sciences (SPSS) for Windows (Version 22.0, SPSS Inc., Chicago, IL, USA). Data distribution was analysed by Kolmogorov Smirnov test. Parametric quantitative data were presented as mean and Standard Deviation (SD). Qualitative data were presented as number (n) and percentage (%). Student's t-test was used for parametric data, and Mann-Whitney U test was used for analysis of non parametric data. Pearson's Chi-square test was used to analyse qualitative data. Receiver Operating Characteristics (ROC) curve analysis was performed to determine the optimum threshold value, sensitivity and specificity of the factors predicting remission. Determinants of non response to treatment were analysed using logistic regression analysis. Two-sided p<0.05 was considered statistically significant for all data.

RESULTS

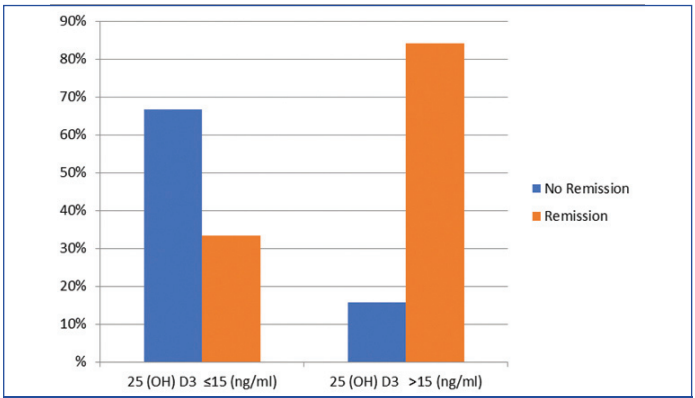
The demographic data, laboratory characteristics and kidney biopsy findings are presented in [Table/Fig-1]. The mean age of the study group (n=56) was 44±13.92 years and 27 of them (48.2%) were male. Twenty-six patients (46.4%) had arterial hypertension (HT), 15 (26.8%) had DM, and 3 (5.4%) had CVD.

Variables	n=56	25(OH)D_3 levels		p-value	Response to therapy		p-value
		Group 1 ≤15 ng/mL n=18	Group 2 >15 ng/mL n=38		No remission n=18	Remission n=38	
Age (year)	44±13.92	42±13.8	46±13.9	0.391	43±13.1	45±14.3	0.625
Gender (male; n, %)	27 (48.2)	11 (61.1)	16 (42.1)	0.184	10 (55.6)	17 (44.7)	0.449
Gender (female; n, %)	29 (51.8)	7 (38.9)	22 (57.9)		8 (44.4)	21 (55.3)	
Co-morbidities (n, %)							
Hypertension	26 (46.4)	5 (27.8)	21 (55.3)	0.054	7 (38.9)	19 (50.0)	0.436
Diabetes mellitus	15 (26.8)	5 (27.8)	10 (26.3)	1.00	6 (33.3)	9 (23.7)	0.524
Cardiovascular disease	3 (5.4)	2 (11.1)	1 (2.6)	0.239	2 (11.1)	1 (2.6)	0.239
Laboratory results							
Glucose (mg/dL)	111±45.4	110±44.7	112±46.3	0.661	116±48.5	109±44.4	0.385
Urea (mg/dL)	48±32.2	46±22.7	50±36.1	0.715	43±21.6	51±36.1	0.405
Creatinine (mg/dL)	1.39±1.08	1.45±0.80	1.36±1.20	0.276	1.44±0.79	1.36±1.21	0.325
eGFR (mL/min/1.73 m^2)	71±30.4	65±28.9	73±31.1	0.364	65±27.7	73±31.5	0.425
Uric acid (mg/dL)	6.8±1.9	7.0±1.7	6.7±1.9	0.958	6.8±1.7	6.7±1.9	0.604
Sodium (mEq/L)	138±4.2	139±4.6	139±4.1	0.614	139±2.4	138±4.8	0.887
Potassium (mEq/L)	4.3±0.4	4.2±0.4	4.3±0.40	0.647	4.3±0.4	4.3±0.4	0.604
Calcium (mg/dL)	8.8±1.1	8.7±0.7	8.8±1.2	0.424	8.6±1.2	8.8±0.,9	0.424
Phosphorus (mg/dL)	3.7±0.7	3.7±0.7	3.7±0.7	0.958	3.7±0.8	3.7±0.6	0.660
Total protein (g/dL)	6.2±1.4	6.0±1.9	6.3±1.1	0.243	5.8±1.2	6.4±1.4	0.075
Albumin (g/dL)	3.4±0.8	3.2±0.9	3.5±0.8	0.304	3.2±0.8	3.5±0.8	0.370
Proteinuria (gr/day)	5.7±3.9	6.8±4.3	5.2±3.8	0.141	7.3±4,6	5.0±3.4	0.092
Total cholesterol (mg/dL)	264±112.8	254±87.6	269±123.8	0.909	257±78.8	268±126.6	0.979
LDL- cholesterol (mg/dL)	172±78.6	171±66.0	172±84.8	0.895	173±59.4	172±87.0	0.605
HDL- cholesterol (mg/dL)	51±15.7	50±18.9	51±14.2	0.568	51±17.5	51±15.0	0.604
Triglyceride (mg/dL)	349±29.1	203±68.7	418±1125.1	0.317	229±76.2	407±1127.0	0.667
WBC (10^3/µL)	8.4±2.5	8.8±3.2	8.2±2.0	0.406	8.7±2.3	8.2±2,5	0.482
Hb (g/dL)	13.1±2.0	12.4±2.1	13.4±1.9	0.068	13.4±2.2	12.9±1.9	0.441
Platelet (10^3/µL)	282±77.9	264±78.4	290±77.4	0.255	291±83.4	277±75.9	0.528
25-(OH) D_3 levels (ng/mL)	17.6±5.5				13.3±2.5	19.6±5.3	**<0.001**
Renal biopsy findings							
IF (%)	30.1±5.5	33.4±5.6	28.6±4.9	**0.002**	36.2±3.5	27.2±3.7	**<0.001**
TA (%)	33.3±7.5	34.5±6.8	32.7±7.8	0.417	37.2±7.4	31.4±6.8	**0.005**
Response to treatment							
No remission	18 (32.1)	12 (66.7)	6 (15.8)	**<0.001**			
Remission	38 (67.9)	6 (33.3)	32 (84.2)				

[Table/Fig-1]: Baseline (at the time of diagnosis) demographic and laboratory characteristics of participants.
eGFR: Estimated glomerular filtration rate; LDL: Low density lipoprotein; HDL: High density lipoprotein; WBC: White blood cell; Hb: Hemoglobin; IF: Interstitial fibrosis; TA: Tubular atrophy
Test applied- Student's t-test, Mann-Whitney U test and Pearson's Chi-squate test. Student's t test was used for parametric data, and Mann-Whitney U test was used for analysis of non parametric data. Pearson's Chi-square test was used to analyse qualitative data
p<0.05 was considered statistically significant for all data

The mean number of glomeruli in kidney biopsies was 19.8±12.6 and the percentage of sclereosis was 42±14.9. Remission was achieved in 38 (67.9%) patients with the treatment applied {complete remission in 32 (57.1%) patients, partial remission in 6 (10.7%)} and remission could not be achieved in 18 patients (32.1%).

Patients with 25(OH)D_3 levels below 15 ng/mL (n=18) formed group1, and those above 15 ng/mL (n=38) were group 2 [Table/Fig-1]. There was no difference between the groups in terms of demographic data and baseline laboratory values (p>0.05). The rate of interstitial fibrosis was higher in group 1 (p =0.002) at the end of first year, 6 (33.3%) patients in group 1 and 32 (84.2%) patients in group 2 achieved remission [Table/Fig-1,2] (p<0.001).



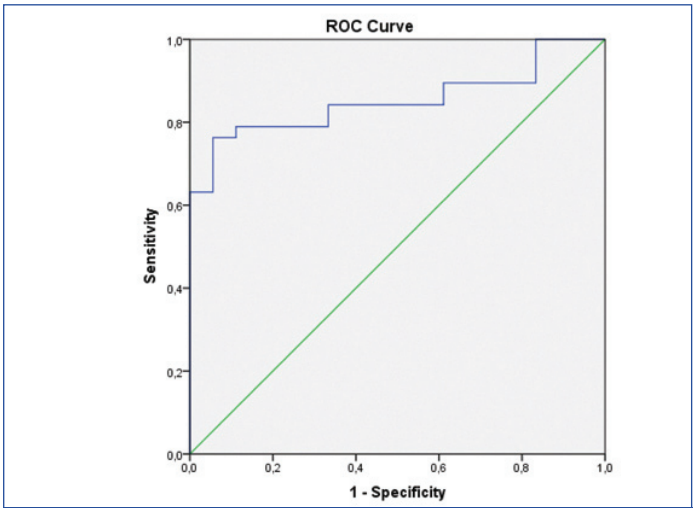
[Table/Fig-2]: Baseline vitamin D levels during biopsy and remission percentage in the first year.

The demographic characteristics and laboratory values at the time of biopsy of the patients, with and without remission, were similar (p>0.05). However, 25(OH)D_3 level was significantly lower, interstitial fibrosis and tubular atrophy were higher in the no remission group compared to the remission group (p<0.01, for all) [Table/Fig-1].

With the ROC analysis, the sensitivity and specificity were defined as 95% and 89% for interstitial fibrosis and 79% and 88% for 25(OH)D_3 level (p<0.001 for both) [Table/Fig-3,4]. As per the binary logistic regression analysis, low vitamin D status and higher interstitial fibrosis were identified as independent predictors of non response to treatment (p=0.036, p=0.004, respectively, [Table/Fig-5].

Variables	AUC	Cut-off	Sensitivity	Specificity	p-value
25(OH)D_3 (ng/mL)	0.852	15	79%	88%	<0.001
IF	0.968	33	95%	89%	<0.001
TA	0.735	38	84%	72%	0.005

[Table/Fig-3]: Results of the ROC analysis to predict remission in the first year by using vitamin D level and IF and TA percentages.
ROC: Receiver operating characteristic IF: Interstitial fibrosis; TA: Tubular atrophy, AUC: Area under the curve; Test applied- ROC analysis and Logistic Regression Analysis; p<0.05 was considered statistically significant for all data



[Table/Fig-4]: Vitamin D Receiver Operating Characteristic (ROC) analysis curve.

Variables	OR (95% CI)	p-value
25(OH)D_3 ≤15 ng/mL	12.8 (1.18-140.19)	0.036
IF >33%	36.9 (3.19-427.41)	0.004
TA >38%	8.5 (0.68-106.70)	0.097

[Table/Fig-5]: Risk factors for no remission in the first year.
IF: Interstitial fibrosis; TA: Tubular atrophy; Test applied-Logistic Regression Analysis; p<0.05 was considered statistically significant for all data

DISCUSSION

The present study, was aimed to examine the relationship between 25(OH)D_3 level and renal prognosis in patients with primary FSGS. It has been shown that patients with higher baseline serum 25(OH)D_3 levels have lower interstitial fibrosis percentage and considerably higher remission rates at the end of the first year. In addition, low basal vitamin D levels have been established to be a predictor of non responsiveness to standard therapy like interstitial fibrosis. To the best of our knowledge, this is the first study to show the relationship between 25(OH)D_3 status and kidney prognosis in FSGS patients.

All of the patients followed in the study clinic were managed to conform to the KDIGO glomerulonephritis clinical practice guideline and response rates were defined according to this protocol [16]. Medical data suggest that spontaneous remission rates of roughly 10% can approach 70% after appropriate treatments in FSGS cases [17]. In this study, comparable to the general literature, complete and partial response rates were calculated as 57.1% and 10.7% at the end of the first year.

The association of vitamin D deficiency with morbidity and mortality in cases of nephrotic syndrome has not yet been defined [18]. Despite these findings, there are a limited number of studies dealing specifically with the relationship between vitamin D and nephrotic syndrome [19,20]. Previously, Li XH et al., argued that 25(OH)D_3 deficiency may indicate serious renal pathological features in the early stage of IgA nephropathy [19]. There are no studies in the literature on FSGS and 25(OH)D_3 deficiency in adults. Among paediatric primary nephrotic syndrome cases, serum 25-hydroxy vitamin D_3 levels were found to be lower in the initial onset and non remission groups than in the remission group [20]. At this point, there is no data on the adult patient population.

Vitamin D deficiency has been shown to be associated with kidney damage in experimental studies. Zhang Y et al., showed that mice lacking the vitamin D receptor developed more severe kidney damage with pronounced tubular atrophy and interstitial fibrosis compared to normal mice [21]. Actually, interstitial fibrosis is a histopathological prognostic factor predicting kidney survival in FSGS patients [22]. Interstitial fibrosis at the time of diagnosis was significantly lower in the patients who achieved remission. Experimental data show that vitamin D analogues reduce albuminuria [23], and vitamin D deficiency activates the renin angiotensin system [24,25]. The positive relationship between vitamin D levels and remission rates in patients with FSGS may have developed through this pathway. Further studies are needed on this subject. There are data suggesting that glomerular damage in FSGS is triggered by immune mechanisms [26,27]. The immunomodulatory effects of vitamin D shown in recent studies [28,29] may be another important reason for the relationship between FSGS and vitamin D. In the present study, the mean 25(OH)D_3 level of 56 participants was 17.6 (±5.5). Vitamin D treatment was administered to patients with deficiency in accordance with the guidelines [30,31]. Serum 25(OH)D_3 levels should be measured regularly in FSGS patients. Adequate vitamin D can effectively prevent the progression of FSGS and reduce the occurrence of glomerular sclerosis.

Limitation(s)

The most important limitation was the small number of participants and the fact that all patients were from a single centre. Another limitation was that the effect of vitamin D treatment on the course of FSGS has was not evaluated.

CONCLUSION(S)

This study demonstrated that low baseline vitamin D levels, as interstitial fibrosis, are an independent predictor of unresponsiveness to standard therapy in patients with primary FSGS. Prospective studies involving more patients are needed to determine whether vitamin D measurement and treatment at the time of diagnosis contribute to the reduction of glomerulosclerosis during FSGS follow-up.

Disclosure: This study is a thesis. 1st researcher is Ç.K., Supervisior is E.G.O., Concept - E.G.O., G.U.O., M.D.A.; Design - Ç.K., E.G.O., G.U.O., H.Ş., T.S., M.D.A.; Data Collection or Processing - Ç.K., H.Ş., T.S.; Analysis and Interpretation - E.G.O., G.U.O., M.D.A.; Literature Search - Ç.K., H.Ş., T.S.; Writing-Ç.K., E.G.O., G.U.O.

REFERENCES

[1] Diniz HF, Romao MF, Elias RM, Romao Junior JE. Vitamin D deficiency and insufficiency in patients with chronic kidney disease. J Bras Nefrol. 2012;34(1):58-63.
[2] Ravani P, Malberti F, Tripepi G, Pecchini P, Cutrupi S, Pizzini P, et al. Vitamin D levels and patient outcome in chronic kidney disease. Kidney Int. 2009;75(1):88-95.
[3] Hamano T, Nakano C, Obi Y, Fujii N, Matsui I, Tomida K, et al. Fibroblast growth factor 23 and 25-hydroxyvitamin D levels are associated with estimated glomerular filtrationrate decline. Kidney Int. 2013;3(5):469-75.
[4] Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: Results of the study to evaluate early kidney disease. Kidney International. 2007;71:31-38.
[5] Kates DM, Sherrard DJ, Andress DL. Evidence that serum phosphate is independently aassociated with serum PTH in patients with chronic renal failure. Am J Kidney Dis. 1997;30(6):809-13.
[6] Pilz S, Iodice S, Zittermann A, Grant WB, Gandini S. Vitamin D status and mortality risk in CKD: A meta-analysis of prospective studies. Am J Kidney Dis. 2011;58(3):374-82.
[7] Deegens JK, Steenbergen EJ, Wetzels JF. Review on diagnosis and treatment of focal segmental glomerulosclerosis. Neth J Med. 2008;66(1):03-12.
[8] Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. American Journal of Kidney Diseases. 2004;44(5):815-25.
[9] Ozturk S, Sumnu A, Seyahi N, Gullulu M, Sipahioglu M, Artan S, et al. Demographic and clinical characteristics of primary glomerular diseases in Turkey. International Urology and Nephrology. 2014;46(12):2347-55.
[10] Stirling CM, Mathieson P, Boulton-Jones JM, Feehally J, Jayne D, Murray HM, et al. Treatment and outcome of adult patients with primary focal segmental glomerulosclerosis in five UK renal units. QJM. 2005;98(6):443-49.
[11] Chun MJ, Korbet SM, Schwartz MM, Lewis EJ. Focal segmental glomerulosclerosis in nephrotic adults: presentation, prognosis, and response to therapy of the histologic variants. Journal of the American Society of Nephrology. 2004;15(8):2169-77.
[12] Jean G, Souberbielle JC, Chazot C. Vitamin D in chronic kidney disease and dialysis patients. Nutrients. 2017;9(4):328.
[13] Zhang Z, Zhang Y, Ning G, Deb DK, Kong J, Li YC. Combination therapy with AT1 blocker and vitamin D analog markedly ameliorates diabetic nephropathy: Blockade of compensatory renin increase. Proc Natl Acad Sci USA. 2008;105:15896-901.
[14] Makibayashi K, Tatematsu M, Hirata M, Fukushima N, Kusano K, Ohashi S, et al. A vitamin D analog ameliorates glomerular injury on rat glomerulonephritis. Am J Pathol. 2001;158:1733-41.
[15] National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003;42(4):01-201.
[16] Kidney Disease: Improving Global Outcomes (KDIGO) a Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. Kidney Int. 2012;2(2):139-274.
[17] Deegens JK, Assmann KJ, Steenbergen EJ, Hilbrands LB, Gerlag PG, Jansen JL, et al. Idiopathic focal segmental glomerulosclerosis: A favourable prognosis in untreated patients? Neth J Med. 2005;63:393-98.
[18] Tian J, Liu Y, Williams LA, Zeeuw D. Potential role of active vitamin D inretarding the progression of chronic kidney disease. Nephrology Dialysis Transplantation. 2007;22(2):321-28.
[19] Li XH, Huang XP, Pan L, Wang CY, Qin J, Nong FW, et al. Vitamin D deficiency may predict a poorer outcome of Ig A nephropathy. BMC Nephrol. 2016;17(1):164.
[20] Zhang X, Wu X, Wang F, Yi Z, Cao Y. Vitamin D levels and vitamin D receptor expression in children with primary nephrotic syndrome. Biomed Res. 2017;28(21):9658-62.
[21] Zhang Y, Kong J, Deb DK, Chang A, Li YC. Vitamin D receptor attenuates renal fibrosis by suppressing the renin-angiotensin system. J Am Soc Nephrol. 2010;21(6):966-73.
[22] Thomas DB, Franceschini N, Hogan SL, Ten Holder S, Jennette C, Falk RJ, et al. Clinical and pathologic characteristics of focal segmental glomerulosclerosis pathologic variants. Kidney Int. 2006;69(5):920-26.
[23] Mizobuchi M, Morrissey J, Finch JL, Martin DR, Liapis H, Akizawa T, et al. Combination therapy with an angiotensin-converting enzyme inhibitor and a vitamin D analog suppresses the progression of renal insufficiency in uremic rats. J Am Soc Nephrol. 2007;18(6):1796-806.
[24] Forman JP, Williams JS, Fisher ND. Plasma 25-hydroxyvitamin D and regulation of the renin-angiotensin system in humans. Hypertension. 2010;55(5):1283-88.
[25] Tomaschitz A, Pilz S, Ritz E, Grammer T, Drechsler C, Boehm BO, et al. Independent association between 1,25-dihydroxyvitamin D, 25-hydroxyvitamin D and the renin-angiotensin system: The Ludwigshafen Risk and Cardiovascular Health (LURIC) study. Clin Chim Açta. 2010;411(17-18):1354-60.
[26] Finch JL, Suarez EB, Husain K, Ferder L, Cardema MC, Glenn DJ. Effect of combining an ACE inhibitor and a VDR activator on glomerulosclerosis, proteinuria, and renal oxidative stress in uremic rats. Am J Physiol Renal Physiol. 2012;302:141-49.
[27] Lang CL, Wang MH, Chiang CK. Vitamin D and immune system from the nephrologists viewpoint. ISRN Endocrinol. 2014;2014:105456.
[28] Kronbichler A, Leierer J, Oh J, Meijers B, Shin JI. Immunologic changes implicated in the pathogenesis of focal segmental glomerulosclerosis. Bio Med Res Int. 2016;2016:215045.
[29] Meyrier A. Focal and segmental glomerulosclerosis: Multiple pathways are involved. Semin Nephrol. 2011;31:326-32.
[30] Isakova T, Nickolas TL, Denburg M, Yarlagadda S, Weiner DE, Gutiérrez OM, et al. KDOQI US Commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evulation, prevention, and treatment of Chronic Kidney Disease Mineral and Bone Disorder (CKD-MBD). Am J Kidney Dis. 2017;70(6):737-51.
[31] Sonmez A, Haymana C, Bayram F, Salman S, Dizdar OS, Gurkan E, et al, TEMD Study Group. Turkish nationwide survey of glycemic and other Metabolic parameters of patients with Diabetes mellitus (TEMD study). Diabetes Res Clin Pract. 2018;146:138-47.

PARTICULARS OF CONTRIBUTORS:

1. Specialist Medical Doctor, Department of Internal Medicine, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
2. Associate Professor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
3. Associate Professor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
4. Specialist Medical Doctor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
5. Specialist Medical Doctor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
6. Professor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ebru Gok Oguz,
Associate Professor, Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey.
E-mail: ebrugokoguz@hotmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Feb 22, 2021
- Manual Googling: May 31, 2021
- iThenticate Software: Jul 07, 2021 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 19, 2021**
Date of Peer Review: **May 19, 2021**
Date of Acceptance: **Jun 11, 2021**
Date of Publishing: **Aug 01, 2021**