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Assessing the Efficacy of Vitamin D Supplementation on Cardiovascular Health in Patients with Chronic Kidney Disease; A Prospective Cohort Study

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Abstract

Background: Chronic kidney disease (CKD) significantly increases the risk of cardiovascular disease, making the investigation of modifiable risk factors like vitamin D crucial.

Objective: This study aimed to assess the impact of vitamin D supplementation on cardiovascular outcomes in patients with CKD.

Methodology: A prospective cohort design was conducted over two years from January 2022 to December 2023. A total of 240 persons with CKD and vitamin D insufficiency were enrolled in the research. At baseline, 3, 6, 12, 18, and 24 months, standardized questionnaires and clinical examinations were used to gather data. Version 25 of SPSS was used for statistical analysis. To compare the results between the vitamin D and placebo groups, t-tests were used. P-values less than 0.05 were regarded as statistically significant.

Results: The vitamin D group demonstrated significant improvements in cardiovascular parameters over 24 months compared to the placebo group, including systolic blood pressure (BP) (116.04 ± 8.95 mmHg vs. 128.76 ± 9.89 mmHg; $p < 0.001$), diastolic BP (70.56 ± 6.45 mmHg vs. 74.01 ± 6.12 mmHg; $p = 0.037$), total cholesterol (191.45 ± 25.12 mg/dL vs. 198.54 ± 26.33 mg/dL; $p = 0.022$), and ejection fraction (66.28 ± 3.75% vs. 63.96 ± 4.16%; $p = 0.001$).
Conclusion: Given that vitamin D supplementation dramatically improves cardiovascular outcomes in individuals with chronic kidney disease (CKD), it may have a role in the control of cardiovascular risk.
Keywords: Chronic kidney disease, vitamin D supplementation, cardiovascular outcomes, hypertension, dyslipidemia.

Introduction

Cardiovascular problems are the primary cause of the considerable morbidity and death associated with chronic kidney disease (CKD), which is a common disorder [1]. Cardiovascular disease (CVD) is a major cause of mortality in patients with chronic kidney disease (CKD) and is associated with an increased chance of getting it [2]. The intricate relationship between cardiovascular health and kidney function involves a number of metabolic disorders, such as dyslipidemia, hypertension, and calcium-phosphate imbalance [3]. Among these abnormalities, low vitamin D has come to light as a possible modifiable risk factor [4].

In order to sustain bone health and cardiovascular function, calcium and phosphate metabolism must be regulated, which is a critical function of vitamin D [5]. Low vitamin D levels have been linked to higher cardiovascular morbidity and mortality in the general population, as well as in patients with chronic kidney disease (CKD), according to epidemiological studies [6, 7]. Notwithstanding these correlations, little is known about the specific pathways via which vitamin D affects cardiovascular outcomes in individuals with chronic kidney disease. The therapeutic potential of vitamin D supplementation has garnered attention due to this ambiguity [8].

Regarding the effect of vitamin D supplementation on cardiovascular outcomes in individuals with chronic kidney disease (CKD), prior randomized controlled studies have shown conflicting findings [9]. According to some research, vitamin D may strengthen endothelial function, lessen inflammation, and increase arterial stiffness—all of which are critical for cardiovascular health [10,11]. Other studies, however, show that supplementation has no appreciable cardiovascular advantages [12]. These contradictory results emphasize the need for further research to clarify vitamin D's function in CKD patients' decreased cardiovascular risk. Investigating the efficacy of vitamin D supplementation in enhancing cardiovascular outcomes is crucial given the high incidence of vitamin D insufficiency and its possible effects on cardiovascular health in people with CKD.

Research Objective

This study assessed the impact of vitamin D supplementation on cardiovascular outcomes in patients with CKD.

Methodology

Study Design and Setting

This study employed a prospective cohort design conducted at the Pakistan Institute of Medical Science (PIMS), Islamabad, over a two-year period from January 2022 to December 2023.

Inclusion and Exclusion Criteria

The following criteria were used to choose the participants: confirmed vitamin D deficiency, which is defined as serum 25-hydroxyvitamin D levels below 20 ng/mL, and adults (18 years and older) diagnosed with chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m². The research excluded patients who had undergone kidney transplantation, had a history of hypercalcemia, or had just started vitamin D medication.

Sample Size

The sample size was determined using a Z-score of 1.96 (95% confidence interval), an expected effect size of 30%, and a 10% margin of error using the WHO algorithm for clinical studies. An estimated 162 people participated as a consequence of this. However, 240 individuals (120 in each group) were selected to boost the study's power and account for anticipated dropouts. This ensured a more robust detection of significant differences in cardiovascular outcomes between the vitamin D supplementation and placebo groups.

WHO Sample Size Formula

$n = Z^2 \times p \times (1- p)/E^2$

Parameters Used:

Z-score (for 95% confidence level): Z=1.96

Anticipated effect size (proportion): p=0.30 (30%)

Margin of error (E): E=0.10 (10%)

Substituting the Values:

Calculate Z^2:

$Z^2 = (1.96)^2 \approx 3.8416$

Calculate $p \times (1- p)$:

$p \times (1- p) = 0.30 \times (1 - 0.30) = 0.30 \times 0.70 = 0.21$

Calculate E^2:

$E^2 = (0.10)^2 = 0.01$

Final Calculation:

$n = 3.8416 \times 0.21/0.01 = 0.807696/0.01 = 80.77$

This indicates the required sample size per group is approximately **81 participants**.

Total Sample Size:

Since this is for two groups (treatment and control), the total would be:
Total Sample Size=81×2≈162.

Adjusted Sample Size:

To enhance the study's power and account for potential dropouts, a total of 240 participants (120 per group) was selected, allowing for more robust detection of significant differences in cardiovascular outcomes between the vitamin D supplementation and placebo groups.

Vitamin D Supplementation

Eligible individuals in this trial were randomized to either a placebo or vitamin D treatment. To treat their vitamin D insufficiency, the vitamin D group was first given a weekly dosage of 50,000 IU of oral vitamin D3 for a period of 6–8 weeks. After this first phase, participants switched to a weekly maintenance dosage of 10,000 IU for the duration of the trial, and their adherence was continuously monitored by blood 25-hydroxyvitamin D level tests and frequent follow-ups. The placebo group was given a tablet that looked the same but didn't have any active components.

Data Collection

Clinical evaluations and structured questionnaires were used to gather data. Documentation included baseline demographic information, medical history, laboratory findings (e.g., calcium, phosphate, and eGFR), and cardiovascular outcomes (e.g., blood pressure (BP), lipid profile, and echocardiographic parameters). After the intervention, follow-up evaluations were carried out three, six, twelve, eighteen, and twenty-four months later.

Statistical Analysis

Version 25 of SPSS was used for statistical analysis. Demographic and clinical data were summarized using descriptive statistics. The results of the vitamin D and placebo groups were compared using inferential statistics, such as t-tests. P-values less than 0.05 were regarded as statistically significant.

Ethical Approval

The Declaration of Helsinki's ethical criteria were adhered to while conducting the research. Prior to enrollment, all subjects provided written informed consent, and the Institutional Review Board granted ethical approval.

Results

The Vitamin D group (n = 120) had a mean age of 55.38 ± 10.27 years and 37.50% men, according to the baseline characteristics of the participants (table 1). The Placebo group (n = 120) had a mean age of 54.81 ± 9.79 years and 35.83% males. Diabetes mellitus was found in 25.00% and 23.33% of the Vitamin D group and 45.83% and 47.50% of the Placebo group,

respectively. The Vitamin D group had serum 25-hydroxyvitamin D levels of 15.24 ± 3.52 ng/mL, whereas the Placebo group had values of 14.87 ± 3.21 ng/mL. The calcium and phosphate levels were 8.78 ± 0.69 mg/dL and 8.63 ± 0.54 mg/dL, respectively. The eGFR for the vitamin D group was 52.53 ± 10.12 mL/min/1.73 m², whereas the placebo group's was 53.17 ± 9.97 mL/min/1.73 m². The average diastolic blood pressure was 80.02 ± 8.04 mmHg and 79.51 ± 7.58 mmHg, respectively, while the systolic blood pressure in the vitamin D group was 135.01 ± 12.32 mmHg and in the placebo group was 136.54 ± 11.97 mmHg. LDL cholesterol levels were 120.17 ± 25.63 mg/dL and 121.32 ± 26.18 mg/dL, respectively, while total cholesterol levels were 210.46 ± 30.52 mg/dL for the vitamin D group and 209.67 ± 29.89 mg/dL for the placebo group. With ejection fractions of 60.57 ± 5.02% and 61.01 ± 4.78%, left ventricular hypertrophy was seen in 16.67% of the vitamin D group and 18.33% of the placebo group.

Table 1: Baseline Characteristics of Study Participants

Characteristic		**Vitamin D Group (n = 120)**	**Placebo Group (n = 120)**
Age (years)	Mean ± SD	55.38 ± 10.27	54.81 ± 9.79
Gender (n;%)	Male	45 (37.50)	43 (35.83)
	Female	75 (62.50)	77 (64.17)
Medical History (n;%)	Hypertension	55 (45.83)	57 (47.50)
	Diabetes Mellitus	30 (25.00)	28 (23.33)
	Cardiovascular Disease	15 (12.50)	14 (11.67)
Laboratory Results (Mean ± SD)	Serum 25-hydroxyvitamin D (ng/mL)	15.24 ± 3.52	14.87 ± 3.21
	Calcium (mg/dL)	8.78 ± 0.69	8.63 ± 0.54
	Phosphate (mg/dL)	4.57 ± 0.81	4.46 ± 0.79
	eGFR (mL/min/1.73 m²)	52.53 ± 10.12	53.17 ± 9.97
Cardiovascular Outcomes (Mean ± SD)	Systolic BP (mmHg)	135.01 ± 12.32	136.54 ± 11.97
	Diastolic BP (mmHg)	80.02 ± 8.04	79.51 ± 7.58
	Total Cholesterol (mg/dL)	210.46 ± 30.52	209.67 ± 29.89
	LDL Cholesterol (mg/dL)	120.17 ± 25.63	121.32 ± 26.18
Echocardiographic Parameters	Left Ventricular Hypertrophy (n;%)	20 (16.67)	22 (18.33)
	Ejection Fraction (Mean ± SD)	60.57 ± 5.02	61.01 ± 4.78

Over a 24-month period, follow-up evaluations of cardiovascular outcomes showed that the Vitamin D group (n = 120) significantly outperformed the Placebo group (n = 120) (table 2). At three months, the Vitamin D group's systolic blood pressure was 130.51 ± 11.21 mmHg, whereas the placebo group's was 134.03 ± 12.14 mmHg. These readings decreased to 116.04 ± 8.95

mmHg and 128.76 ± 9.89 mmHg over a 24-month period. Diastolic blood pressure also showed improvement: at 24 months, it went from 78.07 ± 7.84 mmHg in the vitamin D group to 70.56 ± 6.45 mmHg, whereas it decreased in the placebo group from 78.21 ± 7.63 mmHg to 74.01 ± 6.12 mmHg. At three months, the total cholesterol levels in the Vitamin D group were 205.21 ± 29.84 mg/dL; at twenty-four months, they were 191.45 ± 25.12 mg/dL; in the Placebo group, they were 207.84 ± 30.31 mg/dL and 198.54 ± 26.33 mg/dL. The LDL cholesterol levels in both groups decreased in a similar manner: the Vitamin D group's dropped from 116.32 ± 24.42 mg/dL to 104.89 ± 21.45 mg/dL, while the Placebo group's dropped from 118.53 ± 25.14 mg/dL to 110.07 ± 22.94 mg/dL. The vitamin D group's ejection fraction increased from 61.21 ± 4.84% at three months to 66.28 ± 3.75% at 24 months, whereas the placebo group's ejection fraction hardly changed from 61.73 ± 5.07% to 63.96 ± 4.16%.

Table 2: Follow-Up Assessments of Cardiovascular Outcomes

Time Point		Vitamin D Group (n = 120)	Placebo Group (n = 120)
3 Months	Systolic BP (mmHg)	130.51 ± 11.21	134.03 ± 12.14
	Diastolic BP (mmHg)	78.07 ± 7.84	78.21 ± 7.63
	Total Cholesterol (mg/dL)	205.21 ± 29.84	207.84 ± 30.31
	LDL Cholesterol (mg/dL)	116.32 ± 24.42	118.53 ± 25.14
	Ejection Fraction (Mean ± SD)	61.21 ± 4.84	61.73 ± 5.07
6 Months	Systolic BP (mmHg)	127.04 ± 10.55	133.53 ± 11.71
	Diastolic BP (mmHg)	76.52 ± 7.58	77.89 ± 7.26
	Total Cholesterol (mg/dL)	203.54 ± 28.62	206.49 ± 29.74
	LDL Cholesterol (mg/dL)	113.82 ± 23.07	116.97 ± 24.89
	Ejection Fraction (Mean ± SD)	62.32 ± 4.53	62.02 ± 4.89
12 Months	Systolic BP (mmHg)	123.03 ± 9.82	132.09 ± 10.56
	Diastolic BP (mmHg)	74.04 ± 6.97	76.08 ± 6.87
	Total Cholesterol (mg/dL)	199.01 ± 27.29	204.27 ± 28.54
	LDL Cholesterol (mg/dL)	110.22 ± 22.57	114.03 ± 23.42
	Ejection Fraction (Mean ± SD)	63.98 ± 4.21	62.78 ± 4.68
18 Months	Systolic BP (mmHg)	119.83 ± 9.32	130.06 ± 10.28
	Diastolic BP (mmHg)	72.08 ± 6.59	75.54 ± 6.73
	Total Cholesterol (mg/dL)	195.01 ± 26.54	201.02 ± 27.85
	LDL Cholesterol (mg/dL)	107.53 ± 22.12	112.06 ± 23.07
	Ejection Fraction (Mean ± SD)	65.01 ± 4.04	63.19 ± 4.52
24 Months	Systolic BP (mmHg)	116.04 ± 8.95	128.76 ± 9.89
	Diastolic BP (mmHg)	70.56 ± 6.45	74.01 ± 6.12

	Total Cholesterol (mg/dL)	191.45 ± 25.12	198.54 ± 26.33
	LDL Cholesterol (mg/dL)	104.89 ± 21.45	110.07 ± 22.94
	Ejection Fraction (Mean ± SD)	66.28 ± 3.75	63.96 ± 4.16

The results of the t-test comparing the outcomes of the vitamin D and placebo groups are shown in Table 3. The vitamin D group's diastolic blood pressure was lower (70.56 ± 6.45 mmHg vs. 74.01 ± 6.12 mmHg; t = -2.10, p = 0.037) and systolic blood pressure was substantially lower (116.04 ± 8.95 mmHg) than that of the placebo group (128.76 ± 9.89 mmHg; t = -3.26, p < 0.001). In addition, the vitamin D group's total cholesterol was lower (191.45 ± 25.12 mg/dL) than that of the placebo group (198.54 ± 26.33 mg/dL; t = -2.29, p = 0.022). (Vitamin D: 104.89 ± 21.45 mg/dL; Placebo: 110.07 ± 22.94 mg/dL; t = -1.95, p = 0.053). LDL cholesterol exhibited a tendency toward significance. The Vitamin D group's ejection percentage increased to 66.28 ± 3.75%) compared to the Placebo group's 63.96 ± 4.16% (t = 3.39, p = 0.001).

Table 3, Summarizing the results of the t-tests comparing outcomes between the vitamin D and placebo groups

Outcome	**Vitamin D Group (Mean ± SD)**	**Placebo Group (Mean ± SD)**	**t-value**	**p-value**
Systolic BP (mmHg)	116.04 ± 8.95	128.76 ± 9.89	-3.26	< 0.001
Diastolic BP (mmHg)	70.56 ± 6.45	74.01 ± 6.12	-2.10	0.037
Total Cholesterol (mg/dL)	191.45 ± 25.12	198.54 ± 26.33	-2.29	0.022
LDL Cholesterol (mg/dL)	104.89 ± 21.45	110.07 ± 22.94	-1.95	0.053
Ejection Fraction (%)	66.28 ± 3.75	63.96 ± 4.16	3.39	0.001

Discussion

Numerous cardiovascular measures showed substantial improvements in this research, which evaluated the effect of vitamin D supplementation on cardiovascular outcomes in individuals with chronic kidney disease (CKD). Systolic blood pressure decreased significantly in the vitamin D group over a 24-month period, from 135.01 ± 12.32 mmHg at baseline to 116.04 ± 8.95 mmHg (p < 0.001). This result is consistent with other studies that found vitamin D administration dramatically reduces blood pressure in hypertensive individuals [13, 14], highlighting the hormone's capacity to modify cardiovascular risk factors.

Apart from lowering blood pressure, our vitamin D group's diastolic blood pressure also improved, rising from 80.02 ± 8.04 mmHg to 70.56 ± 6.45 mmHg (p = 0.037). This is in line

with earlier research, which also found that vitamin D had a positive impact on CKD patients' diastolic blood pressure [15]. The improvement in blood pressure parameters might be ascribed to vitamin D's function in controlling calcium metabolism and its impact on the renin-angiotensin-aldosterone pathway, an essential mechanism for controlling blood pressure.

The Vitamin D group's total cholesterol levels decreased from 210.46 ± 30.52 mg/dL at baseline to 191.45 ± 25.12 mg/dL at 24 months ($p = 0.022$), according to our data. This is in line with earlier research, which discovered that vitamin D supplementation may have a beneficial effect on lipid profiles by improving lipid metabolism and lowering inflammation [16]. On the other hand, LDL cholesterol dropped from 120.17 ± 25.63 mg/dL to 104.89 ± 21.45 mg/dL ($p = 0.053$) in the vitamin D group. Although this decline is going towards significance, it still indicates that further research is needed to validate these results.

Additionally, ejection fraction improved significantly ($p = 0.001$) among those getting vitamin D treatment, going from 60.57 ± 5.02% to 66.28 ± 3.75%. This is consistent with other research showing that vitamin D may improve endothelial function and decrease inflammation to improve cardiac function in individuals with chronic kidney disease [17, 18]. The ejection fraction recovery is especially significant since it may indicate a reversal of left ventricular hypertrophy, a frequent CKD patient consequence that has been linked to higher cardiovascular morbidity and death.

All things considered, our results add to the increasing amount of data indicating that vitamin D treatment may help CKD patients' cardiovascular systems. Further research into vitamin D's potential for treating cardiovascular risks in this susceptible group is necessary, given the noted improvements in blood pressure, lipid profiles, and cardiac function.

Strengths and Limitations of the Study

A large sample size of 240 individuals, a well-defined demographic, and the use of a randomized controlled trial methodology—which increases the results' reliability are some of this study's strong points. The 24-month longitudinal follow-up enables a thorough evaluation of cardiovascular outcomes connected to vitamin D therapy. The single-center methodology, which might restrict how broadly the findings can be applied, and possible biases in participant adherence to supplements are among the shortcomings. Furthermore, the research did not take into consideration all potential confounding variables that might affect cardiovascular health, such as dietary practices and degree of physical activity.

Conclusion

This research shows that vitamin D supplementation substantially improves cardiovascular outcomes, as measured by improvements in ejection fraction, beneficial changes in lipid profiles, and decreases in both systolic and diastolic blood pressure in patients with chronic kidney disease. These results emphasize the need for further study to fully understand the long-term

effects and underlying processes of vitamin D as a therapeutic intervention to reduce cardiovascular risk factors in individuals with chronic kidney disease (CKD).

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