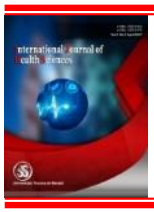

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The Effect of Cholecalciferol Supplementation on PTH and Increasing the Glomerular Filtration Rate in Kidney Transplant Patients at King Faisal Specialist Hospital and Research Center

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Abstract

Background: The association between oral cholecalciferol and GFR has been identified in various renal transplant populations around the globe. This study aimed to evaluate the effect of oral cholecalciferol supplementation on the GFR and serum PTH levels, with other parameters in the Saudi kidney transplant population. Methods: A retrospective observational study was conducted on a cohort of 174 kidney recipients who underwent transplantation and had serum 25-Hydroxy VD level tests performed (2018-2022) at King Faisal Specialist Hospital and Research Center in Jeddah, KSA. Generalized and linear mixed effects regression models were conducted. Results: The percentage of GFR >60 (25.86% vs 78.16%, P<.0001) and VD insufficiency (< 30 ng/mL) (36.21% vs 6.90%, P<.0001) were significantly different between pre-& post-transplant periods, respectively. After adjustment, significant changes were found in post-transplant GFR, hemoglobin levels, serum creatinine levels, blood urea nitrogen levels, hematocrit levels, PTH levels, and VD 25-Hydroxy from the baseline. Calciferol 1000/2000 IU and 50,000 IU (P<.0001) were significantly more effective in increasing the odds of having GFR >60 as compared to other supplements (P=0.75). Conclusions: VD supplementations may be particularly beneficial in improving kidney function in kidney transplant patients, as this contributed to normalizing GFR levels and creatinine levels and reducing PTH levels.

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Contents

1 Introduction

Vitamin D deficiency frequently occurs after renal transplantation; however, several studies have demonstrated that serum concentration of vitamin D in healthy people should be maintained above 30 ng/ml serum 25-OH (Pludowski et al., 2018). Vitamin D concentration helps to regulate the blood calcium level and prevent serum parathyroid hormone (PTH) levels from increasing (Courbebaisse et al., 2009; Yang et al., 2007; Evenepoel et al., 2016).

Renal transplant recipient (RTR) patients have vitamin D concentrations below the recommended level in the months or years after transplant (Courbebaisse et al., 2023), possibly due to insufficient sun exposure or lack of vitamin D supplementation after transplantation. Moreover, growth factor-23 secretion increased in RTR and increased the catabolism of 25-OH vitamin D by immunosuppressive medications (Durak & Karakan, 2020). Vitamin D deficiency was found to be associated with a high risk of fractures, osteoporosis, cancer, heart diseases, and impaired kidney function (Pludowski et al., 2022; Bartl, 2023).

Chronic Kidney Disease (CKD) is characterized by a gradual loss in the structure and kidney function for at least three months. The Glomerular Filtration Rate (GFR) is used to screen for CKD, as it measures how well kidneys filter waste and fluids from blood (Graciolli et al., 2017; Impellizzeri et al., 2014). A GFR of less than 60 ml/min might indicate the presence of kidney disease (Webster et al., 2017). In Saudi Arabia, there are over twenty thousand patients on dialysis and nine thousand eight hundred ten patients under follow-up after kidney transplantation (Arabia, 2023).

A recent intervention study was conducted from January 2017 to January 2018 to assess the efficacy of oral cholecalciferol on patients with vitamin D deficiency who are diagnosed with CKD and who are given oral vitamin D 50,000 IU once a week. In this study, the level of vitamin D was increased over three months, and there was a significant decrease but weak correlation of creatinine, phosphate, and PTH levels with vitamin D ($p<0.05$). The study provides evidence supporting the considerable efficacy of oral vitamin D supplementation in CKD patients (Memon et al., 2022).

An Italian study investigated the efficacy of cholecalciferol (10,000 IU) once a week for 12 months on CKD patients with vitamin D deficiency. This study suggested a possible association between vitamin D levels and reducing PTH serum levels. The study recommended oral cholecalciferol supplementation in CKD patients (Cupisti et al., 2015).

A Turkish study enrolled two groups – one received 400 IU/ day and the other group received 600/ day orally – to investigate the effects of low doses of cholecalciferol and calcium supplementation in bone loss in renal transplant patients. A one-year follow-up was associated with an increase in vitamin D levels and a decrease in PTH levels (Sahin et al., 2008).

Understanding the potential benefits of cholecalciferol supplementation in enhancing kidney function may have a significant impact on the treatment and management of kidney transplant recipients (Rule et al., 2013; Price & Finney, 2000). It may also help healthcare and clinical practice in optimizing vitamin D status and possibly improve kidney transplant patient outcomes. Overall, the rationale for this investigation is to address a clinically relevant question regarding the impact of cholecalciferol supplementation on kidney function in kidney transplant patients and potentially contribute to the existing knowledge on the management of posttransplant complications (Meier-Kriesche et al., 2000; Dimitroulis et al., 2009). To our knowledge, no previous studies have investigated the effect of oral cholecalciferol on GFR and PTH in renal transplant patients in Saudi Arabia. We hypothesized that oral cholecalciferol may normalize PTH levels and GFR levels. We also hypothesized that the serum level of vitamin D might be improved in our cohort (Carter et al., 2004; Dusso, 2011). We performed a retrospective study to evaluate the effect of oral cholecalciferol supplementation on increasing the GFR and reducing PTH levels, as well as improving other laboratory parameters in kidney transplant patients in Jeddah, Saudi Arabia.

2 Materials and Methods

Study design

A retrospective study was conducted and collected the data for patients before the kidney transplant in 2018 and after the kidney transplant in 2022 from the medical files at King Faisal Specialist Hospital and Research Center in Jeddah, Saudi Arabia. Research protocols were approved by the unit of the Biomedical Ethics Research Committee of King Faisal Specialist Hospital and Research Center. The protocols were carefully explained to the hospital, and Informed Consent for Research (10139 V.1) was obtained from KFSHRC

Study cohort

A total of 174 kidney transplant patients (male and female) with ages between 18-59 were included in this investigation and received kidneys from both living-related donors and cadaveric donors. That data was determined based on the available data within a specific time frame and eligible patients that are already available from past medical records or databases. Inclusion and exclusion criteria established clear criteria for participant selection, and researchers can minimize selection bias. In this study, the inclusion criteria were Saudi kidney transplant patients with no need for dialysis. Exclusion criteria were non-Saudi, suffering from chronic diseases, pregnant and lactating, and need for dialysis, see **Figure 1.**

Measures

Demographic profiles such as gender, age, and body mass index (BMI) were retrieved from the medical files by the Citrix Program. At the baseline, laboratory test results and oral cholecalciferol supplementations (calciferol 1000/2000 IU, 50,000 IU, and other supplements) were collected from the patient's record before a kidney transplant operation in 2018. We also collected laboratory test results (2022) four years after a kidney transplant operation. Laboratory test results included HbA1C, serum 25(OH)D, GFR, PTH, urea, creatinine, albumin, ionized calcium, and phosphate, all of which were measured according to standard procedures for data collection to reduce measurement bias. The primary measure of kidney function is the GFR. It was assessed before and after the transplant operation by the estimated GFR according to the equation from the Modification of Diet in Renal Disease study as recommended by K/DOQI guidelines: 170 × creatinine mg/dL −0.999 × age/year − 0.176 × 0.762 (if patient is female) × urea mg/dL − 0.170 × albumin g/dL +0.38 (Lentine et al., 2017). A GFR over 60 ml/min/1.73m^2 is adequate and normal. However, any significant decline of the GFR of less than < 60 ml/min/1.73m^2 can be an early indicator of kidney disease.

Statistical analysis

Data analysis was analyzed using SAS version 9.4 (SAS Institute, Cary, NC). No missing data or dropouts were reported in this study. Pre- and post-kidney transplant GFR and laboratory measurements were summarized using percentages and mean ± SD in **Table 1**. McNemar's test and paired t-tests were used when appropriate. We employed generalized and linear mixed effects regression models to examine the changes in GFR and laboratory parameters pre- and post-kidney transplant while controlling for recipients' demographic characteristics as potential confounders (**Table 2**). This will assess the impact of using any vitamin D supplements (as all 174 recipients received them) using GFR and laboratory parameters. **Sensitivity analyses**: we also assessed the impact of different vitamin D supplements (1000/2000 IU, 50,000 IU, other) on GFR and laboratory measurements by adding an interaction term: Supplement × Time (**Table 3**). This analysis followed a post hoc test using Tukey's multiple comparisons. A p-value (P) of 5% or lower indicates statistical significance.

3 Results and Discussions

3.1 Results

Cohort characteristics and subgroup analyses

Among all eligible renal transplant recipients (n=174), the mean age was 39.6 ± 10.3 (range 19-59 years), and 55.75 percent were male. In the unadjusted analyses (**Table 1**), there was a higher prevalence of insufficient vitamin D in pre- versus post-kidney transplant (36.21% vs. 6.90, P< 0.001). The percentage of GFR > 60 mL/min/1.73 m^2 was significantly lower in pre- versus post-kidney transplant (25.86% vs. 78.16%, P< 0.001). We noted a significant increase in hemoglobin levels, hematocrit levels, serum calcium levels, and vitamin D 25-Hydroxy levels in the posttransplant period as compared to the pretransplant period (P < 0.0001), while blood urea nitrogen levels, serum creatinine levels, PTH levels, and serum potassium levels were significantly greater in the pretransplant period as compared to the posttransplant period (P < 0.0001).

Adjusted analyses

After adjustment for recipients' demographic characteristics as potential confounders, the use of any vitamin D supplements was significantly associated with the log odds of having GFR > 60 (B=2.381, P <.0001) (**Table 2**). In the posttransplant period, our recipients had significantly greater hemoglobin levels (B=18.833, P<0.0001), hematocrit levels (B=0.056, P<0.0001), serum calcium levels (B=0.102, P<0.0001), and vitamin D 25 Hydroxy levels (B=20.255, P<0.0001) than in the pre-transplant period. However, blood urea nitrogen levels (B=-8.926, P<0.0001), creatinine levels (B=-427.79, P<0.0001), PTH levels (B=-265.490, P<0.0001), and serum potassium levels (B=-0.466, P<0.0001) became significantly lower in the posttransplant period. Female recipients had significantly lower hemoglobin levels (B=-9.504, P<0.0001), hematocrit levels (B=-0.025, P=0.001), creatinine levels (B=-106.480, P=0.001), albumin levels (B=-1.453, P=0.005) than male recipients. Age was significantly correlated with vitamin D 25-Hydroxy levels (B=0.339, P=0.009). After adjustment for recipients' demographic profile, the use of calciferol 1000/2000 IU (B=3.277, P =0.001) and calciferol 50.000 IU (B=1.438, P =0.030) were significantly associated with increased log odds of having GFR > 60 (**Table 3**).

Figure 2 shows calciferol 1000/2000 IU (P<.0001) and 50,000 IU (P<.0001) were significantly more effective in increasing the odds of having GFR > 60 as compared to the other supplements (P = 0.749). Calciferol 1000/2000 IU was significantly associated with increased hemoglobin levels (B=13.703, P =0.050) and decreased creatinine levels (B=-223.010, P =0.045). **Figure 3** shows a significant increase (pre vs post) in hemoglobin levels with 1000/2000 IU (P<.0001), 50,000 IU (P<.0001), and an insignificant increase with the other supplements (P=0.404). **Figure 4** shows that there was a significant decline (pre vs post) in serum creatinine levels with calciferol 1000/2000 IU (P<.0001), 50,000 IU (P<.0001), and the other supplements (P=0.0358). The use of calciferol 1000/2000 IU (B=-7.941, P =0.013) and calciferol 50,000 IU (B=-7.552, P =0.011) were significantly associated with decreased thyroid-stimulating hormone levels.

3.2 Discussion

This study focused on exploring the effect of cholecalciferol supplementation on PTH levels and its potential to increase GFR in a cohort of kidney transplant patients in Saudi Arabia. Our findings demonstrated that 25(OH)D levels significantly increased with vitamin D_3 treatment, demonstrating that the supplement dosages were appropriate among kidney transplant recipients. In this study, we expected that the serum level of vitamin D would be improved in transplant patients after four years. Baseline (35.3±13.1 nmol/L) and after four years (55.5±24.0 nmol/L) with a p-value of ($P < 0.001$), which means increasing vitamin D in patients after kidney transplantation. Moreover, no adverse effect of vitamin D toxicity was reported from any patient in our cohort. A prospective international study conducted at the Indus Hospital in Karachi, Pakistan, evaluated the effect of oral cholecalciferol in chronic kidney disease patients with vitamin D deficiency. Patients were given 50,000 IU of oral vitamin D per week if there was a severe deficiency < 10 ng/ml, and for others with less severe symptoms, 10-25 ng/ml every other week for three months. The improvement in vitamin D deficiency was observed after three months. A weak negative significant correlation between phosphate, creatinine, and PTH was found. However, there is a positive significant efficacy of oral vitamin D in CKD. Research showed that more than 80% of cases with CKD have a high deficiency of vitamin D (Filipov et al., 2015), the same as >80% of non-transplant patients having a high frequency of vitamin D insufficiency of low serum 25(OH)D levels (Ngai et al., 2014).

According to the Institute of Medicine (IOM) in 2011, the Adequate Intake (IA) of vitamin D in infants is estimated to be 400 IU/day, and from age 1 for all life stage groups, it is estimated to be 600 IU/day, except aged 71 and older, and for whom the RDA is 800 IU/day (Ross, 2011). Vitamin D is synthesized in the skin after exposure to sunlight, as a major source of vitamin D, and can be obtained from dietary sources. Vitamin D is converted into two hydroxylations to be in active form: calcitriol. Calcitriol plays a crucial role in calcium homeostasis, and deficiency of this hormone can result in secondary hyperparathyroidism (Fraser, 2022).

Several studies have demonstrated that cholecalciferol supplementation effectively reduces PTH levels among kidney transplant patients (Tsujita et al., 2020; Bover et al., 2021; Battaglia et al., 2023). By providing an optimal level of vitamin D, cholecalciferol helps to improve calcium absorption and thus lowers PTH secretion (Janoušek et al., 2022). In kidney transplantation, patients have a common issue in the development of secondary hyperparathyroidism, characterized by elevated PTH levels, and face challenges related to bone health and calcium metabolism (Jannot et al., 2020). In the current study, PTH level results indicated that there were significant differences among patients before and after a kidney transplant, baseline (403.19±435.26) ng/L and after four years (137.69±95.91) ng/L, ($p<.001$). This is consistent with our analysis after adjustment for demographic profiles which show a significant decrease of 265.490 in the PTH levels within the four-year posttransplant. The decrease in PTH levels may be related to administration of vitamin D supplementations. In the kidney, there is an overlapping between PTH and calcium receptors when the PTH has a direct effect on calcium metabolism, increasing the calcium extracted from the GFR in the kidney by PTH action (Bhattarai et al., 2020).

The GFR is a measure of kidney function and is obtained by the plasma or urinary clearance rate at which the kidneys filter waste products from the blood (Cusumano et al., 2021). Additionally, impaired kidney function after transplantation can lead to a decrease in the GFR (Campion et al., 2022). As for GFR levels in this study, results indicated significant differences among patients before and after a kidney transplant. At the baseline 25.86% of our cohort had GFR ≥ 60 and after four years: 78.16% had GFR ≥ 60, (<0.001), which means increasing GFR in patients after kidney transplantation may be related to increased vitamin D levels.

Supplementing with oral cholecalciferol has been studied for its ability to raise GFR in kidney transplant recipients (Battaglia et al., 2020). This is consistent with our study: cholecalciferol 1000/2000 IU ($P<.0001$) and 50,000 IU ($P<.0001$) were associated with increased odds of having GFR > 60. Vitamin D receptors are present in various renal cell types, including podocytes, mesangial cells, and tubular epithelial cells. Activation of these receptors by calcitriol may directly affect renal function, including vasodilation of the renal arterioles and modulation of the renin-angiotensin-aldosterone system (Lei et al., 2020). These actions have the potential to increase renal blood flow and improve GFR. While the evidence regarding the direct effect of cholecalciferol supplementation on GFR in kidney transplant patients is limited, some studies have reported positive outcomes (Cianciolo et al., 2021; Yin et al., 2022). These studies have suggested that cholecalciferol supplementation may contribute to an improvement in renal function, as reflected by an increase in GFR.

However, further research is needed to establish a clear causal relationship and determine the optimal dosage and duration of cholecalciferol supplementation to achieve these benefits.

In a study of sixty hemodialysis patients (HD) with PTH level >300pg/ml, patients were randomly divided into two groups, a control (placebo) group and a study group (cholecalciferol) with 2 mcg/day. In this study, at 16 weeks there was a significant increase in vitamin D and a decrease in PTH levels (Zheng et al., 2016).

Bidirectional calcium and phosphate fluxes regulate the phosphate and calcium homeostasis that occurs in three organs: kidney, intestines, and bone (Feher, 2017). As for Ca levels in our study, results indicated that there was a significant increase in calcium levels in patients after kidney transplantation.

A study conducted in 2018 evaluated the association between the 25-hydroxyvitamin D and GFR and the urine albumin/ creatinine ratio (UACR) in 4,948 Korean adults. The results reveal that there is a positive association between vitamin D deficiency with increased UACR levels and a decrease in GFR (Kim et al., 2018). Our study shows cholecalciferol 1000/2000 IU associated with a significant decrease in creatinine levels and maintained normal results in posttransplant (Figure 4).

In 2015, an observational study in 435 Renal Transplant Recipients was conducted, investigating whether 25(OH) or 1,25$(OH)_2$ D levels are associated with mortality, renal function decline, and graft failure in RTR. A positive association was found between 1,25(OH)D2 and mortality and between 1,25$(OH)D_2$ and graft failure. Severe VD deficiency was mainly associated with GFR decline (Keyzer et al., 2015; Hothefa et al., 2022).

Calcitriol, the active form of vitamin D, decreases the VD receptor and acts on the kidney, intestines, and bones to adjust the level of calcium in the blood. This is similar to the PTH which is secreted when the level of calcium is low. PTH helps to regulate the level of calcium in the blood by calcitriol[22].The current study has some limitations as the data was not collected specifically for the research, resulting in some unavailable clinical information, potential selection bias, and reliance on existing medical records. Also, retrospective observational study limits our ability to establish causal relationships. All the data were collected from King Faisal Specialist Hospital and Research Center, which limits the findings to only one center. The sample size may be relatively small, however, despite these, our study observes and explains the importance of vitamin D supplementations in kidney transplant recipients. A therapeutic intervention may be recommended in kidney transplant patients with low levels of vitamin D, nonetheless, a large multicenter study should be encouraged to confirm our findings.

4 Conclusion

Vitamin D supplementations may be particularly beneficial in improving kidney function in kidney transplant patients, as it contributes to the normalizing of GFR levels and creatinine levels as well as reducing PTH levels. Further research is warranted to explore the mechanisms underlying these effects and to optimize vitamin D supplementation strategies in the transplant population.

Author Contributions

Fatimah Mohammed Ali Yousef: Conceptualization, Project administration, Supervision, Writing - Review & Editing. **Haneen Abdul Rahman al Farra, Mohammed Abdul Jawad alFarra:** Conceptualization, Methodology, Data Cleaning, Writing - original draft. **Waal Habhab and Lama Hefnie**: Supervision, Writing - Review & Editing. **Arwa Mohammed Shukri Turkistani:** Writing - Review & Editing.

Conflict of interest
The authors report no conflicts of interest in this work.

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Table 1
Patient demographic, vitamin D insufficiency, and glomerular filtration rate pre- and post-kidney transplant data

	Pre-transplant		Post-transplant		P
	n	%	n	%	
Male	97	55.75			
Female	77	44.25			
Supplement calciferol 1000/2000 IU	52	29.89			
calciferol 50.000 IU	101	58.05			
Other IUs	21	12.07			
Vitamin D insufficiency (< 30 ng/mL) No	111	63.79	162	93.10	<0.001*
Yes	63	36.21	12	6.90	
GFR ≥ 60 No	129	74.14	38	21.84	<0.001*
Yes	45	25.86	136	78.16	
	Mean	SD	Mean	SD	
Age	39.62	10.30			
BMI	25.85	5.25			
Glucose	6.83	3.36	6.31	2.92	0.072
Hemoglobin	114.98	21.90	133.81	20.29	<0.001*
Hematocrit	0.36	0.07	0.42	0.06	<0.001*
Blood urea nitrogen	15.29	13.94	6.36	9.14	<0.001*
Creatinine	533.93	423.39	106.14	92.24	<0.001*
Albumin	42.69	4.69	42.89	3.97	0.611
Parathyroid hormone	403.19	435.26	137.69	95.91	<0.001*
Thyroid-stimulating hormone	2.37	1.37	3.07	12.31	0.458
Sodium	137.39	3.56	137.99	4.27	0.131
Potassium	4.52	0.78	4.05	0.54	<0.001*
Calcium	2.25	0.27	2.35	0.15	<0.001*
Phosphorous PO4	1.39	0.58	2.36	12.03	0.283
Vitamin D 25-Hydroxy	35.29	13.11	55.54	24.01	<0.001*

* Indicates statistical significance (p=0.05)

Table 2
Predictors of laboratory parameters among kidney transplant recipients who received vitamin D supplement (any dose of IU)

	GFR ≥ 60		Glucose		Hemoglobin		Hematocrit		Blood urea nitrogen		Creatinine		Albumin		Parathyroid hormone		Thyroid stimulating hormone		Sodium		Potassium		Calcium		Phosphorous PO4		Vitamin D 25 Hydroxy	
	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P
Age	-0.02	0.17	0.01	0.47	-0.11	0.37	0.00	0.75	0.003	0.97	0.36	0.83	-0.01	0.59	-2.95	0.10	-0.02	0.63	0.012	0.588	0.005	0.177	-0.002	0.18	0.06	0.220	0.34	0.005*
BMI	-0.03	0.26	0.05	0.20	0.44	0.07	0.001	0.14	-0.05	0.70	2.52	0.44	-0.13	0.009*	3.41	0.33	-0.16	0.09	0.063	0.161	0.000	0.993	0.003	0.27	-0.12	0.213	0.005	0.981
Female	0.298	0.29	-0.64	0.10	-9.50	<.0001*	-0.03	0.001*	-0.54	0.67	-106.48	0.001*	-1.45	0.005*	15.14	0.67	-0.60	0.53	-0.007	0.987	-0.049	0.506	0.021	0.40	-1.24	0.185	-3.29	0.158
Male	Ref																											
Post-transplant	2.38	<.0001*	-0.52	0.07	18.83	<.0001*	0.07	<.0001*	-8.93	<.0001*	-427.79	<.0001*	0.20	0.61	-265.49	<.0001*	0.70	0.46	0.598	0.131	-0.466	<.0001*	0.102	<.0001*	0.97	0.284	20.26	<.0001*
Pre-transplant	Ref																											

* Indicates statistical significance (p=0.05)

Table 3
Predictors of laboratory parameters among kidney transplant recipients who received different doses of Ius

		GFR ≥ 60		Glucose		Hemoglobin		Hematocrit		Blood urea nitrogen		Creatinine		Albumin		Parathyroid hormone		Thyroid-stimulating hormone		Sodium		Potassium		Calcium		Phosphorous PO4	
		B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P
Age		-0.017	0.272	0.01	0.488	-0.09	0.424	0.000	0.849	0.006	0.933	0.34	0.838	-0.015	0.557	-2.92	0.11	-0.02	0.70	0.02	0.51	0.005	0.18	-0.002	0.14	0.07	0.15
BMI		-0.035	0.230	0.05	0.210	0.44	0.060	0.001	0.143	-0.05	0.700	2.27	0.486	-0.129	0.012*	3.23	0.36	-0.15	0.10	0.06	0.19	-0.001	0.94	0.003	0.25	-0.13	0.17
Female		0.312	0.279	-0.64	0.098	-9.48	<.0001*	-0.025	0.001*	-0.54	0.676	-107.35	0.001*	-1.439	0.006*	14.52	0.68	-0.58	0.54	-0.02	0.96	-0.05	0.49	0.02	0.39	-1.27	0.17
Male		Ref																									
Post-transplant		0.797	0.175	-0.91	0.278	11.14	0.059	0.033	0.070	-13.20	0.001*	-279.14	0.003*	0.043	0.970	-153.74	0.1	7.45	0.006*	0.43	0.71	-0.41	0.05	0.06	0.32	4.41	0.09
Pre-transplant		Ref																									
Supplement																											
Calciferol 1000/2000 IU		-1.110	0.047*	0.22	0.786	-15.65	0.003*	-0.044	0.008*	-2.653	0.388	212.2	0.007*	-1.254	0.255	130.03	0.11	0.35	0.88	0.17	0.87	0.23	0.19	0.01	0.86	0.39	0.86
Calciferol 50.000 IU		-1.107	0.030*	0.10	0.891	-12.27	0.013*	-0.036	0.019*	-4.588	0.108	153.22	0.036*	-0.309	0.762	96.17	0.21	0.12	0.96	-0.39	0.68	0.25	0.12	0.03	0.52	-0.02	0.99
Other IUs		Ref																									
Supplement x Time																											
Calciferol 1000/2000 IU	Post-transplant	3.277	0.001*	0.32	0.742	13.7	0.050*	0.041	0.057	2.535	0.557	-223.01	0.045*	0.900	0.507	-150.99	0.17	-7.94	0.013*	0.21	0.88	0.03	0.92	0.04	0.56	-2.37	0.44
Calciferol 50.000 IU	Post-transplant	1.438	0.030*	0.49	0.588	6.19	0.337	0.018	0.362	6.057	0.132	-141.27	0.169	-0.189	0.880	-114.79	0.27	-7.55	0.011*	0.19	0.88	-0.12	0.60	0.05	0.51	-4.71	0.10
Other IUs	Pre-transplant	Ref																									

* Indicates statistical significance (p=0.05)

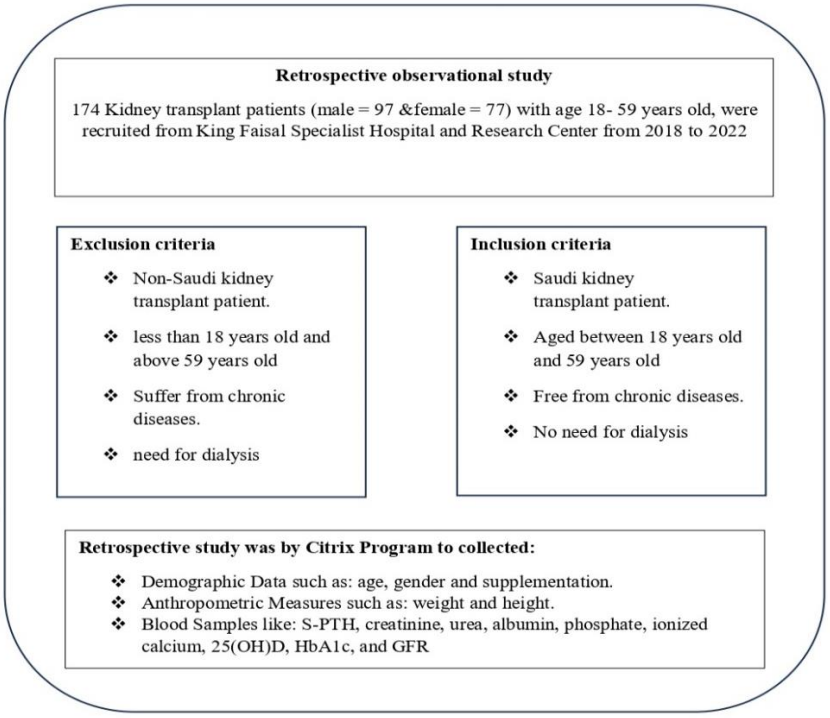

Figure 1. Flow chart of the study sample selection

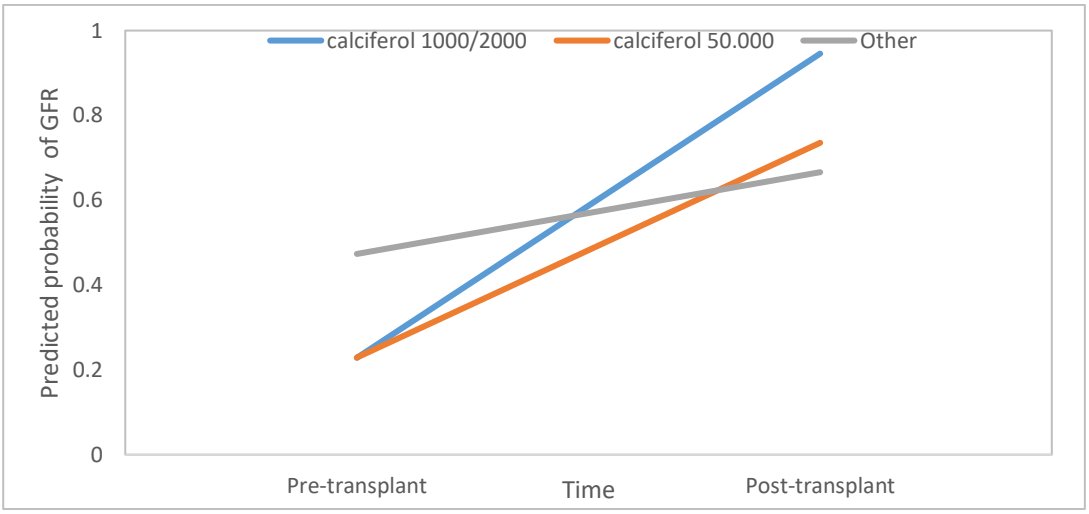

Figure 2. Impact of vitamin D supplementation on the odds of having GFR > 60

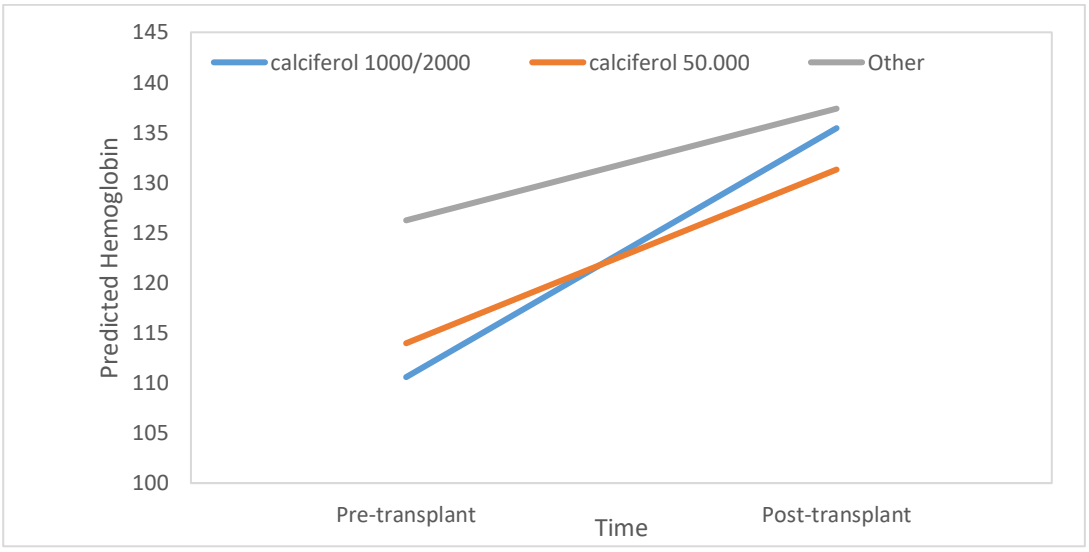

Figure 3. Impact of vitamin D supplementation on hemoglobin levels

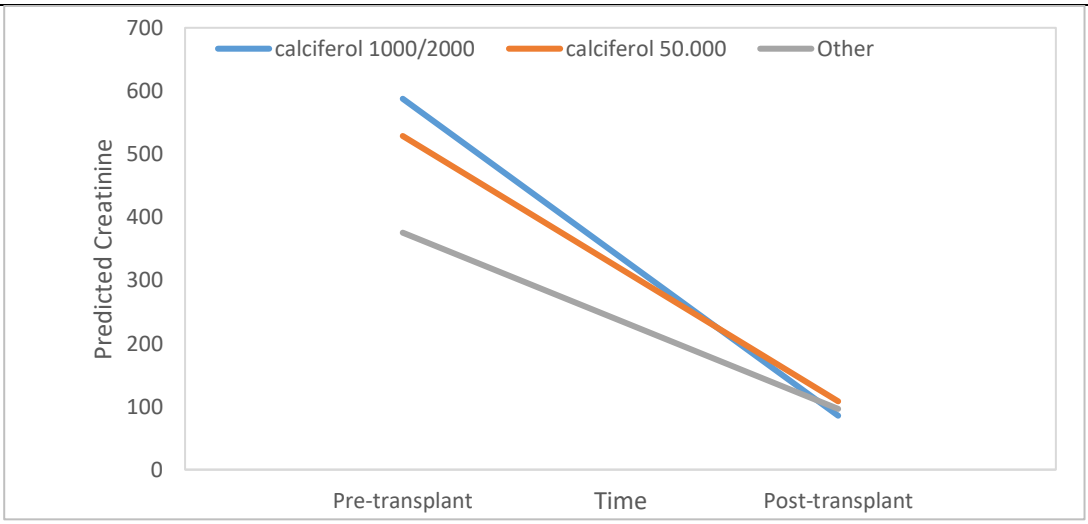

Figure 4. Impact of vitamin D supplementation on serum creatinine levels

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