Clinical Medicine and Health Research Journal (CMHRJ)
Volume 04, Issue 05, September - October, 2024
Page No. 1007-1013,

Research Article

Investigation the Role of Calcium and Vitamin D3 And Some Biochemical Parameters in Patients with Renal Failure of Renal Failure

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Received: 15 September, 2024 : Accepted: 20 October, 2024 : Published: 30 October 2024

Abstract:

Coronavirus Disease 2019 is a primarily respiratory illness that can cause thrombotic disorders. Elevation of D-dimer is a potential biomarker for poor prognosis in COVID-19, though optimal cutoff value for D-dimer to predict mortality has not yet been established. This study aims to assess the accuracy of admission D-dimer in the prognosis of COVID-19 and to establish the optimal cutoff D-dimer value to predict hospital mortality.

Clinical and laboratory parameters and outcomes of confirmed COVID-19 cases admitted to four hospitals in Kathmandu were retrospectively analyzed. Admitted COVID-19 cases with recorded D-dimer and definitive outcomes were included consecutively. D-dimer was measured using immunofluorescence assay and reported in Fibrinogen Equivalent Unit (μg/ml). The receiver operating characteristic curve was used to determine the accuracy of D-dimer in predicting mortality, and to calculate the optimal cutoff value, based on which patients were divided into two groups and predictive value of D-dimer for mortality was measured.

D-dimer levels were higher in COVID-19 patients and were related with markers of inflammation, and after treatments, D-dimer levels decreased which was synchronous with hsCRP levels in patients with good clinical prognosis. Also, the low correlation between Padua VTE score and D-dimer levels weakened the role of D-dimer in the prediction of thrombosis.The abnormal changes of D-dimer and inflammatory factors suggest that aggressive anticoagulant therapy might be needed.

Introduction

Calcium is the most abundant and important element in the human body and has several essential functions, the most important of which are muscle contraction, dilation and contraction of blood vessels, secretion of hormones and enzymes, and it is a key factor in stopping bleeding because it is a cofactor in the clotting mechanism (Standing, 1997). Calcium is available in three forms in blood plasma and is in a balanced form with each other as follows: -

1- Ionic characteristic (++ Ca) and constitutes 50% - 60% of blood plasma.
2- Bound with protein (albumin) and constitutes 30% - 45% of blood plasma.
3- In a complex form with organic ions such as citrate at a rate of 5%-10%. These structural forms help develop balance when changes occur in plasma proteins and blood pH (Miller et al., 2001). Calcium is absorbed from the small intestine and from there it reaches the blood. The highest absorption of calcium is 60% in adolescents and children, and absorption decreases with increasing age. Vitamin D increases the effectiveness of calcium absorption, and calcium absorption also increases during pregnancy. The parathyroid hormone calcitonin has an effect on the level of calcium in the plasma, as it works to increase the level of ionized calcium (Ca+) in the blood plasma by increasing the demolition processes and dissolving part of the bone tissue, as for the hormone calcitonin, which is secreted by specialized cells in the thyroid gland, it works to reduce the level of ionized calcium in the blood and decreases its reabsorption from the kidney. It is stimulated by an increase in ionized calcium in the plasma, which is increased in cases of renal failure and tuberculosis (Hyperparathyrodosim). Calcium deficiency occurs in several pathological conditions such as tetany (causing an increase in muscle tension), osteomalcia, pregnancy, and sprue.

Materials and Methods

Blood

The volume of blood drawn ranged around 10 cm3 from healthy and ill people and turned into divided based on the type of exam. 5 cm3 was located in plastic tubes with covers containing an anticoagulant (EDTA) for the reason of engaging in blood group determination tests, white blood cell count (WBCs cunt), hemoglobin concentration (Hb), percentage of packed red blood cell volume (PCV) and erythrocyte sedimentation rate (ESR) (Powers, 1989).

Serum Preparation

The serum was received by way of putting the final volume of the drawn blood as in the preceding paragraph in a plastic tube with a decent cover and free of anticoagulant and leaving the blood at a temperature of 25°C until it clotted and then placing it in a centrifuge for 10 minutes. The serum (filter) was

withdrawn using a micro pipette and placed in easy, sterile tubes and saved frozen at a temperature of 20°C. The serum was used to conduct hormonal and biochemical checks.

Hematological tests

The first part of the drawn blood was taken and located in tubes containing EDTA for the purpose of conducting the following tests on it (Powers, 1989).

Measuring the percentage of the volume of packed blood cells (PCV)

Capilary tubes were used, 75 mm long and with an internal diameter of about 1 mm, and two-thirds of the capillary tube was filled with blood using the capillary property, then one of its ends was close using manufactured clay. The tube was place in a microcentrifuge at 0.005 rpm for 5 minutes. The separation amid the plasma column and the blood cells was then slow using a special ruler or a hematocrit reader (Heamatocrit Reader) and the percentage of the volume of the packed blood cells was read.

Measurement of Hemoglobin Determination (Hb)

The Hb value was calculate by dividing the result of the PCV value by 3.3, since hemoglobin represents 1/3 of the volume of the red blood cell (Powers, 1989).

Measurement of white blood cell count (WBCs Total Leucocytes Count)

The method of counting white blood cells was used using Turke's Fluid dilution solution, which was prepared by adding 1 cm^3 of a 1% aqueous solution of Gentian Violet dye to 1.5 cm^3 of concentrated glacial acetic acid. The components were mixed well, then 98 cm^3 of distilled water was added to the mixture (Powers, 1989).

Method of work

Put 0.4 ml of Turke's solution in a small tube, then add 0.02 cm^3 of the drawn blood, shake the mixture well, then put a drop of it on the edge of the slide cover placed above the blood cell counter, left for two minutes and examined at the minimum power of 10x, then counted in the four large squares that form the corners of the blood cell counter slide.

Calculations:

Number of cells = Number of cells counted × 50 = cells per cubic millimeter of blood

Estimation of calcium ion level in blood serum: Determination of Serum Calcium

Basic principle:

The calcium ion in the blood serum was measured according to the method mentioned in the kit prepared by the French company

Biomerieux, which bears the number 1011801.

As calcium reacts with the red complex compound forming a complex in the basic solution O_cresol phtaleine in which we measure the calcium concentration.

Solutions used:-

Reagent(1) 2-Amino -2-methyl -1- 500 mmol/l*

Buffer solution proponol

Reagent(2) Gresolphtaline cowps 0-62mml/l *

69mmol/l - hydroxy quinoleine8

Reagent(3) Calcium standard 2.5 mmol/l*

(10 mg/dc)

Preparation of materials used: -

Mix a certain volume of Buffer solutions (R1) with the same volume of color solutions. (R2)

Method of work

Substant	Blank	Standard	sample
Standard	/	20ml	/
sample	/	/	20 ml
Reagent (1)	1 ml	1 ml	1 ml

The tubes were mixed well and left for five minutes at room temperature and read at a wavelength of 570 nm and according to the calcium as Next:-

2.5 x Calcium concentration =

Standard mmol/l reading

Results and Discussion

Data of result study showed there is high significant different ($p<0.05$) between gender, age groups, and smoking of patients. The males patients scored lowest percentage (30.0%) than females (70.0%). The age group 21-40 years scored highest percentage (60.0%), while >60 years age group scored lowest percentage (5.0%). The no smoker patients scored lowest percentage (80.0%) than females (20.0%). (table 1).

Table 1; frequency and percentage of gender, age groups and smoking of patients were calculated by chi-square test.

	Value	Count	Percent	P value
Gender	male	6	30.0%	p<0.001***
	female	14	70.0%	
Age groups	1-20	2	10.0%	p<0.001***
	21-40	12	60.0%	
	41-60	5	25.0%	
	>60	1	5.0%	
Smoking	no	16	80.0%	p<0.001***
	yes	4	20.0%	

The conducted results show high significant different ($P<0.05$) between creatinine, urea, , TSH, Ca, and vitamin D3 with study groups .We noticed high levels of inine, urea, , and TSH, in patients (1.75±0.33, 128.16±44.60, and 5.47± 1.72) respectively, than healthy .In contrast, the levels of Ca and vitamin D3 were low in patients (7.93±0.82, and 18.38± 6.28) than healthy (table 2 and figure 1).

Table 2; comparative mean levels of biochemical parameters between study groups were calculated by student t test.

Groups		N	Mean	SD	P value
creatinine	patients	20	1.75	0.33	P<0.05*
	healthy	10	0.88	0.19	
urea	patients	20	128.16	44.60	P<0.001***
	healthy	10	37.40	5.68	
TSH	patients	20	5.47	1.72	P<0.05*
	healthy	10	3.10	0.57	
Ca	patients	20	7.93	0.82	P<0.05*
	healthy	10	10.20	0.63	
Vitamin D3	patients	20	18.38	6.28	P<0.001***
	healthy	10	34.20	7.52	

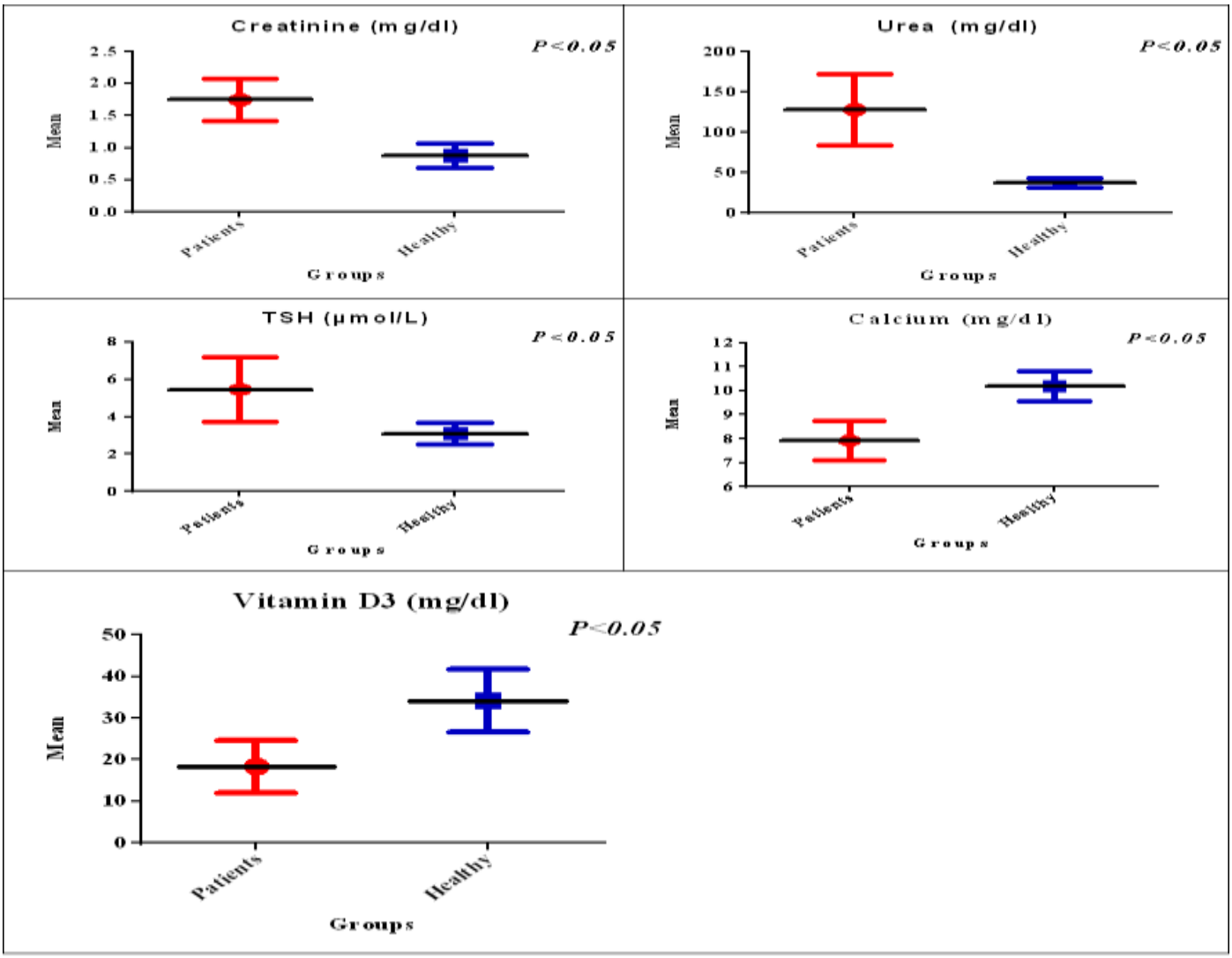

Figure 1; comparative mean levels biochemical parameters between study groups

Results of present study showed there is positive and negative correlations among hematological parameters in patients. Importantly, there positive significant correlation between urea and creatinine (r= 0.445* sig.= 0.049) (r= 0.631* sig.= 0.001) (table 3).

Table 3; correlation relationship among hematological parameters were calculated by Pearson correlation.

		Creatinine	TSH	vitamin
Creatinine	Pearson coefficient	1	.054	.066
	Significant		.822	.782
urea	Pearson coefficient	.445*	-.195	.014
	Significant	.049	.410	.954
Ca	Pearson coefficient	-.251	-.379	-.006
	Significant	.285	.099	.979
vitamin	Pearson coefficient	.066	.147	1
	Significant	.782	.535	

Receiver operator characteristic (ROC) curve of parameters

Results of present study showed the creatinine, urea, and TSH scored high sensitivity (89%, 80%, and 90%) and specificity (100%, 90%, and 80%) respectively with significant difference ($p<0.05$) in screening patients with renal failure (figure 2).

Table 4; ROC curve, sensitivity and specificity of variables

Variable	AUC	p value	C.I. 95%		Sensitivity %	Specificity %
			Lower	Upper		
creatinine	.860	0.001***	.731	.989	89	100
urea	.750	0.001***	.560	.940	80	90
TSH	.900	0.001***	.778	1.000	90	80
Ca	.008	0.001***	.000	.028	20	10
Vitamin D3	0.21	0.001***	0.19	1.21	25	19

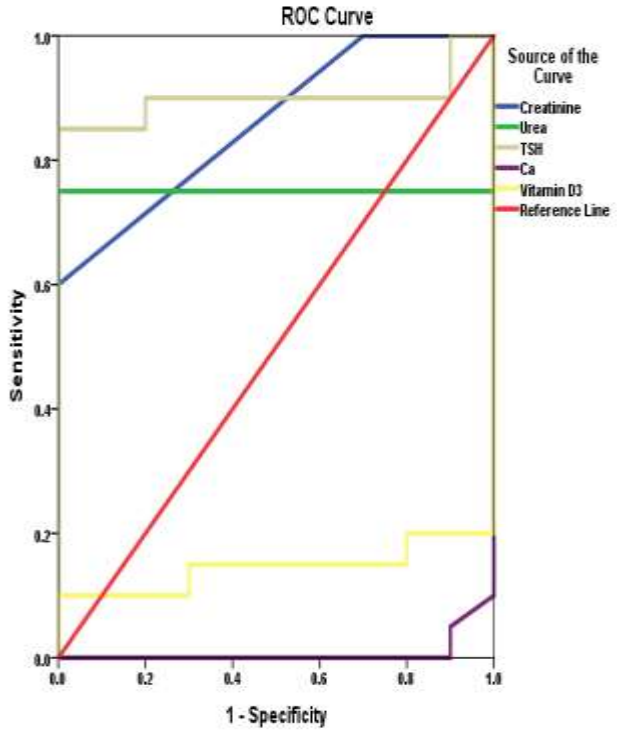

Figure 2; ROC curve, sensitivity and specificity of variables

Discussion

The look at carried out shows enormous variations between CRF and fitness in terms of gender and those results are constant with the findings (Hödlmoser et al., 2020). Sex changes are of essential rank in greatest sicknesses, which includes chronic kidney disease (CKD). Exhibit one-of-a-kind signs and symptoms and signs, reply in a different way to treatment and tolerate/manipulate the disorder in another way. However, a gendered technique in CKD prevention and remedy and in studies has been in large part neglected (Kubo et al., 2016). Awareness of chronic kidney ailment is lower among girls inside the United States than among guys. The slim gender hole in latest years and findings on CKD consciousness by serum creatinine suggest that healthcare professionals previously relied on serum creatinine to tell patients about their circumstance, however in recent years have come to apply eGFR, which bills for decrease creatinine ranges. Inside the blood serum of ladies due to decreased muscle tissue (Hödlmoser et al., 2020).

Based on age, our consequences indicated that CKD increases with age. A cohort look at observed that with growing age, CKD remission and loss of life had been much the potential impact of population growing older at the burden of CKD (Liu et al., 2021). Chronic kidney sickness (CKD) is regularly viewed as a continual, irreversible, lifelong circumstance (Eknoyan et al., 2013). Stabilization of kidney characteristic over the years is visible because the great-case situation for someone with persistent kidney sickness genuine improvement because of chance element change with the aid of The path to remedy or spontaneous recovery (Glassock et al., 2017). With increasing age, the hazard of development or kidney failure in moderate-to-severe CKD tiers decreased, whilst regression became as a minimum as in all likelihood as development or kidney failure in moderate-to-excessive CKD stages (Ravani et al., 2020).

One of the maximum striking aberrations as a result of urea is insulin resistance, a mechanism related to cardiovascular disorder and mortality (Budlaj et al., 2006). If any unique method to selectively decrease urea attention is evolved, evaluation of insulin resistance may be the first surrogate outcome to estimate whether or not this intervention may be effective, and at the equal time definitely verify in the scientific placing the toxicity of urea, that's pretty full-size. So some distance it's been validated experimentally. Blood urea ranges upward thrust in instances in which kidney clearance is reduced (in acute and chronic kidney failure/impairment) because of kidney harm. Urea may additionally growth in other situations now not related to kidney sickness together with upper gastrointestinal bleeding, dehydration, catabolic states, and excessive-protein diets. Urea might also decrease in hunger, a low-protein weight loss program, and severe liver sickness. Serum creatinine is an extra correct assessment of kidney feature than urea. However, urea is expanded early in kidney ailment (Liang et al., 2019). We be aware a lower in urea degrees after repeated dialysis, and those effects are consistent with the results of Ajam, (2020). The effects of the have a look at showed that patients with persistent kidney sickness have a high level of urea in the blood relative to the improvement of the sickness and it's far strongly stricken by the catabolic nation or excessive protein consumption, which results in elevated manufacturing of other wastes from protein catabolism, and an growth in the degree of creatinine in patients with persistent kidney sickness that They are diagnosed as low no. Of functioning nephrons, this leads to a decrease inside the glomerular filtration fee, and causes a sizeable decrease inside the renal float of water and solutes (Amin et al., 2014). Urea manufacturing is directly proportional to day by day protein intake, and restriction of nutritional protein consumption effects in reduced urea production (Seki et al., 2019). Given the close relationship between urea level and dietary protein intake, evaluation of dialysis adequacy may be considered incomplete without assessment of nutritional consumption (Canaud et al., 2019). Higher urea levels, but not calculated serum osmolarity (cSosm) tiers, had been associated with unfavorable renal results unbiased of glomerular filtration price (eGFR), suggesting that blood urea (BUN) may be a useful marker for predicting the development of kidney sickness. (Seki et al., 2019).

Among all metabolic byproducts, urea, creatinine, and potassium ranges are critical indicators for beginning dialysis (Evangelidis et al., 2017). Our results showed better degrees of urea and creatinine in the blood of sufferers with kidney failure as compared to healthful humans, as urea is the main nitrogenous substance from metabolic waste, that's specifically inside the liver and is excreted via urine. As an end result of the imbalance and deficiency in kidney function because of kidney failure, there may be a decrease within the excretion of urea from the body, which ends up in its accumulation in the blood, and its attention will increase (Chen et al., 2020). Researchers additionally indicated that a high degree of urea displays a

failure of the renal filtration characteristic, which be contingent on the quantity of proteins spent and the charge in their obliteration further to the harshness of kidney failure (Nisha et al. 2017).). High urea attention does now not be contingent handiest on kidney feature, but may be due to different factors consisting of increased quantity of protein consumed by way of sufferers, muscle damage, as occurs in instances of starvation, extended fee of protein catabolism, similarly to continual liver disorder. The boom in urea attention reflects the formation of urea in the blood of patients, which signifies the very last stage of persistent renal failure (Alain et al. 2010).

The excessive concentration of creatinine within the blood of sufferers with kidney failure is because of the reality that creatinine is a metabolic residue that is clearly excreted via the urine and is an end result of kidney failure and the inability of the kidneys to carry out its work, inclusive of filtration and excretion of urine. Creatinine. As a result of the lower within the quantity of working nephrons in sufferers with kidney failure who go through dialysis, it reduces the glomerular filtration charge. It also reasons a massive lower inside the kidney's secretion of water and soluble substances, so the stages of urea and creatinine upward thrust. (Ewan et al. 2013). Based at the effective correlation among serum and saliva creatinine ranges determined within the statistics outcomes, the authors accept as true with that saliva analysis might be used as a non-invasive alternative to blood evaluation for the diagnosis of continual kidney disorder in youngsters (Renda, 2017).

The urea-to-creatinine ratio turned into now not related with the occurrence of temporary or unrecoverable rheumatoid arthritis. In difference, stratification rendering to the urea-to-creatinine ratio classifies a collection of patients with a higher risk of lengthy-time period mortality which includes sufferers with continual rheumatoid arthritis. Non-convalescing rheumatoid arthritis is strongly related to long-time period all-purpose mortality after hospitalization for infection. The urea-to-creatinine ratio need to now not be used to predict prerenal azotemia, however identifies a set of sufferers at multiplied risk of long-time period mortality after infection, unbiased of rheumatoid arthritis and sepsis (van der Slikke et al., 2020). .

The contemporary observe showed higher tiers of TSH in sufferers with continual kidney sickness in comparison to healthy controls, and these consequences have been regular with the effects of Rhee et al., (2016). A developing body of proof suggests that hypothyroidism is a threat thing for CKD, progression of CKD, and a better danger of death in sufferers with kidney sickness. Rigorous studies are needed to determine the impact of thyroid hormone substitute at the improvement of kidney ailment, cardiovascular disorder, and mortality, which may shed mild on the causal results of hypothyroidism in CKD (Rhee et al., 2016). Thyroid dysfunction, hypercholesterolemia, low HDL ldl cholesterol, undesirable LDL ldl cholesterol, and hypertriglyceridemia are not unusual in sufferers with CKD. The improvement of continual kidney sickness is followed by way of a upward thrust in hypothyroidism and cardiovascular ailment (Khatiwada et al., 2015).

A preceding look at showed that older adults found an affiliation among hypothyroidism and the improvement of chronic kidney disorder in ladies and individuals with out diabetes. This locating shows that thyroid function should be evaluated periodically in aged adults to hit upon people with ordinary thyroid feature. In addition, people with poor kidney function ought to robotically have thyroid assessments due to the fact they're much more likely to develop hypothyroidism. Thyroid and kidney function have to be carefully monitored in humans with incredibly ordinary TSH levels because they may be vulnerable to worsening kidney characteristic. (Chuang et al., 2017).

Hypothyroidism is an endocrine complication this is fantastically familiar in patients with persistent kidney disease (CKD). A huge frame of proof has proven that there's a bidirectional relationship among thyroid disorder and kidney disorder, yet there are nevertheless many closing gaps in understanding regarding the clinical management of CKD patients with hypothyroidism, which include the ones receiving dialysis. Kidney and peritoneal dialysis. Given that hypothyroidism has been associated with severa unfavourable outcomes which include better danger of demise, cardiovascular ailment, bad health-associated nice of lifestyles, and changed frame composition in both non-CKD sufferers and patients with CKD, there is a need To future studies to decide the appropriate examination. And diagnostic and treatment procedures on this population (Narasaki et al., 2021.(

A recent study showed that low unfastened triiodothyronine (FT3) levels are an impartial danger element for the development of DKD and DKD. Free thyroxine (FT4) ≥4.30 pmol/L in guys and −3.99 pmol/L in girls will substantially growth the hazard of developing kidney ailment in sufferers with type 2 diabetes (Yang et al., 2022.(

The contemporary study confirmed decrease calcium levels in sufferers with continual kidney disease as compared to healthy controls, and those outcomes were constant with the effects of Dhondup and Qian, (2017). The dating among nutritional calcium and the development of CKD appears marginal, besides that if it's miles responsible for hypercalcemia/hypercalciuria, it can result in stone formation, high blood strain, and kidney failure. Dietary intakes may also impact serum degrees, and the resulting low or excessive serum tiers are recognized to be associated with improved mortality and progression of chronic kidney sickness. However, the principle subject in patients with CRF is immoderate calcium consumption and cargo because of the hazard of calcifications and detrimental cardiovascular effects (Janmaat et al., 2018).

The modern examine confirmed lower ranges of vitamin D3 in patients with continual kidney sickness in comparison to healthful humans, and those outcomes have been consistent with the consequences of Vahdat, (2020). There are extraordinary reports concerning the situation of Vit. D in extraordinary international locations. On the alternative hand, clinical studies stated observations in sufferers with kidney ailment. Levine et al. Mineral metabolism abnormalities have been pronounced in early continual kidney disease (CKD). In

those patients, the level of the active shape of the vitamin turned into determined. D became better than the glomerular filtration price (GFR) (Levinet al., 2007).

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