**The Libyan International Medical University**

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# Correlation between hypervitaminosis D and renal failure

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## Abstract

Over the past two decades, interest in vitamin D has increased significantly, Besides playing important roles in calcium homeostasis and bone and muscles and overall health vitamin D is made in our bodies through a series of processes that start when our skin is exposed to the sun's ultraviolet (UV) radiation, Based on guidelines by the Institute of Medicine, recommended dietary allowances for vitamin D are 600 IU/day for those aged between 1 and 70 years and 800 IU/day for those aged 71 and above, extremely high doses of vitamin d supplements over an extended period of time cause vitamin d to build up in the blood which leads to serious condition known as hypervitaminosis D[(2)] ,the main consequence of vitamin D toxicity is a buildup of calcium in your blood (hypercalcemia) High levels of vitamin D metabolites in the blood increases the amount of calcium that the intestine absorbs, which can cause nausea and vomiting, weakness, and frequent urination Symptoms might progress to bone pain and kidney problems nephrocalcinosis can occur if this condition is severe, it can cause permanent kidney damage and eventually renal failure[(1)].

## Introduction :

vitamin D is a group of fat-soluble secosteroids its an essential nutrient that your body needs for many vital process The main source of vitamin D is in human skin it is produced endogenously ,The epidermal layer of human skin synthesizes vitamin D when exposed to UV radiation in the presence of sunlight a form of vitamin d called choleciferol is synthesized from a derivative of the steroid cholesterol in the skin, the liver converts cholecalciferol to calcidiol which is then converted to calcitriol (the active chemical form of the vitamin) in the kidneys through binding to vitamin d receptor (VDR) , vitamin d facilities intestinal absorption of calcium it stimulates the expression of a number of proteins involved in transporting calcium from the lumen of the intestine across the epithelial cells and into blood The best-studied of these calcium transporters is *calbindin*[(2)].

It also stimulates absorption of phosphate and magnesium ions to enable normal mineralization of bone Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by vitamin D. vitamin D can be also obtained from food and very few foods have enough vitamin D to reach recommended daily intake there are two main ways to get sufficient amounts of vitamin D in the body are to expose bare skin to sunlight and take vitamin D supplements, supplements are very common and both vitamin D2 and vitamin D3 can be taken in supplement vitamin D3 is produced in response to sun exposure and is found in animal products whereas vitamin D2 occurs in plants[(2)].

According to the Food and Nutrition Board at the Institute of Medicine of The National Academies, the recommended dietary allowance of vitamin D for people aged (1-70) is 600 IU each day and 800 IU for those aged over 70 years Doctors may prescribe higher doses to treat medical conditions such as vitamin D deficiency [(2)], diabetes, and cardiovascular disease, for a short period of time. Daily use of high-dose vitamin D supplements for several months is toxic also Some prescription medications used to treat high blood pressure (thiazide diuretics) and heart diseases (digoxin) can cause an increase in vitamin D in the blood.,Also taking antacids for a

long time, and isoniazide an antituberculosis medication, can cause elevated levels of vitamin D patients under these conditions are more likely to develop hypervitaminosis D it occurs when blood levels rise above 150ng/ml, toxicity isn't common it's a state when markedly elevated 25 (OH)D levels (>150 ng/ml) coinciding with hypercalcemia Hypercalciuria and very low PTH activity , Most of the significant side effects associated with vitamin D toxicity are related to hypercalcemia , it is an excess of calcium in the blood , Initial signs and symptoms of hypervitaminosis D may be similar to other hyper calcemic states and include generalized weakness it also affects the gastrointestinal tract and cause recurrent vomiting and abdominal pain, hypercalcemia affects kidney function Excess calcium in the bloodstream Can bind with phosphate and form crystals that deposit in soft body tissues ,The kidney is especially vulnerable to calcium deposits because of its role as a filter and its many small passageway, calcium deposits in kidney tissues [(2)].

Nephrocalcinosis can occur if this condition is severe, Clinicians frequently treat patients with Vitamin D for diverse clinical symptoms to improve the general health and to reduce the frailty of elderly and these doses of vitamin d may at times be inappropriately high which lead to toxicity and it induces acute kidney injury ,Acute renal failure or acute kidney injury develops rapidly, usually in less than a few days, acute renal failure occurs when your kidneys suddenly become unable to filter waste products from your blood it loses their filtering ability, dangerous levels of wastes may accumulate, and your blood's chemical makeup may get out of balance [(2)].

## Aim of study:

The aim of this report is to discuss the important role of vitamin D and it synthesis during exposure to sunlight and also to discuss about vitamin d toxicity (hypervitamanosis d) and its causes and the complications following the toxicity and its adverse effects mainly on kidney.

## Materials and methods:

Data was collected of 19 patients with Vitamin D toxicity-induced AKI seen over two years (January 2014–January 2016) from a single tertiary care center in Sher-i Kashmir Institute of Medical Sciences, Srinagar, India.[1]Patients were referred to the Nephrology department to diagnose the cause of AKI, and of these, patients fulfilling the criteria for Vitamin D toxicity were included. Vitamin D toxicity was defined as elevated serum calcium level (>105 mg/dL) with 25(OH) D level >150 ng/mL. Detailed clinical history was obtained in all patients. Laboratory evaluation included measurement of serum calcium, 25(OH) D, intact parathyroid hormone (iPTH) [1], phosphorus, blood urea, and serum creatinine. Serum iPTH was measured using a chemiluminescent microparticle assay (Abbott architect i1000 SR; normal laboratory range 15–70 pg/mL), and serum 25(OH) D was measured using a chemiluminescent microparticle assay (Abbott architect i1000 SR). We also searched electronic laboratory database at our center for a total number of 25(OH) D, estimations made and their results between years 2014 to 2016[1].

## Result:

Of the 19 patients studied, eight were male, and 11 were female. Median (range) age was 64 (45–89) years , this figure summarizes the clinical and biochemical characteristics of the 19 patients [Table 1][(1)] .

| Case number | Age/gender | 25(OH)D (ng/ml) Diagnosis of AKI | Creatinine (mg/dl) (eGFR) |
|---|---|---|---|
| 1 | 84/F | 462 | 1.9 |
| 2 | 66/M | 301 | 3.7 |
| 3 | 65/M | 504 | 2.8 |
| 4 | 76/F | 601 | 2.7 |
| 5 | 61/M | 433 | 3.6 |
| 6 | 69/F | 605 | 1.9 |
| 7 | 65/F | 190 | 2.7 |
| 8 | 71/F | 204 | 3.5 |
| 9 | 49/M | 354 | 2.8 |
| 10 | 56/F | 389 | 3.7 |
| 11 | 45/M | 344 | 2.2 |
| 12 | 56/F | 444 | 3.3 |
| 13 | 51/M | 308 | 5.4 |
| 14 | 59/M | 322 | 3.9 |
| 15 | 64/F | 399 | 2.1 |
| 16 | 89/M | 988 | 4.9 |
| 17 | 72/F | 654 | 3.3 |
| 18 | 61/F | 308 | 3.2 |
| 19 | 58/F | 653 | 4.4 |

## DISCUSSION:

Vitamin D toxicity-induced acute kidney injury is almost always an iatrogenic problem and is totally preventable. There are unusual case reports of Vitamin D intoxication and renal failure secondary to the use of over-the-counter supplements[1], Accidental consumption of very high doses of Vitamin D has also been reported to cause AKI, Our case series is an example of an overambitious attempt to correct Vitamin D deficiency, All the cases were prescribed Vitamin D much beyond the recommended pharmacological doses Moreover, most of the patients were prescribed intramuscular injections of Vitamin D containing very high dose (600,000 IU) at frequent intervals (daily, alternate day or weekly, etc). Parenteral preparations of Vitamin D should be avoided unless there is evidence of malabsorption, and none of our patients had any suggestion of malabsorption Seven patients developed AKI with only oral intake of Vitamin D, and another seven developed AKI with only injectable preparation of Vitamin D, but they received very high doses, such as 60,000 IU oral daily or on alternate days over one to three months and 600,000 IU of intramuscular Vitamin D daily or alternate day or weekly[1].

The presenting clinical manifestations were nausea and vomiting ($n$ = 11), altered sensorium ($n$ = 7), constipation ($n$ = 9), acute pancreatitis ($n$ = 2), renal failure ($n$ = 16), acute on chronic kidney disease ($n$ = 3), and weight loss ($n$ = 2) ,Enteral or parenteral overcorrection of Vitamin D deficiency was the cause of Vitamin D toxicity-induced renal failure in all cases, All the patients were prescribed Vitamin D by their primary care doctor for various indications: bone pains ($n$ = 6), generalized aches and pains ($n$ = 6), fatigue ($n$ = 5), and myalgia's ($n$ = 2) [1] ,Mode of Vitamin D administration was intramuscular injections of Vitamin D3 (each containing 600,000 IU) in seven patients, oral sachets/capsules (each containing 60,000 IU) in seven patients and combined oral and intramuscular in five patients. None of the patients presented with clinical or laboratory evidence of malignancy or any granulomatous disease, either during evaluation at hospital or during subsequent follow-up, for the next three months. They had no history of consumption of foods fortified with Vitamin D3. All patients had normal computerized scan/magnetic resonance imaging scans of the brain, a total of 19 patients were hospitalized for the management of AKI associated with Vitamin D toxicity[1].

The exact toxic dose of Vitamin D has not been established. The Institute of Medicine report concluded that doses below 10,000 IU/day are not usually associated with toxicity, whereas doses equal to or above 50,000 IU/day for several weeks or months are frequently associated with toxic side effects including documented hypercalcemia-induced AKI, Most of the reports of Vitamin D toxicity have documented Vitamin D intake of >40,000 IU/day. Single high doses in the pediatric population (Stoss therapy) were associated with hypercalcemia and probably hypervitaminosis D [(1)].

In this report, significant variability was noticed in the amount of Vitamin D intake and serum 25(OH) D , the cumulative Vitamin D dose was above 240000 IU[(1)]. The mean cumulative Vitamin D dose received in our case series was 6274737 IU over a mean period of nine weeks (range: 5 weeks to 14 weeks), which corresponds to a mean Vitamin D intake of 99599 IU/day. This highlights that high doses may be associated with Vitamin D toxicity Vitamin D intoxication results in elevation of the plasma concentrations of various metabolites of Vitamin D3: 25(OH)D3, 24,25(OH) 2D3, 25,26(OH)2D3 and 25(OH)D3-26,23-lactone [(1)].

## CONCLUSION

Our case series demonstrates the emergence of renal failure due to Vitamin D toxicity as an increasingly common clinical problem. Irrational use of Vitamin D in megadoses resulted in AKI (renal failure) in all cases ,To prevent iatrogenic Vitamin D toxicity, awareness should be increased among health-care providers regarding the toxic potential of mega doses of vitamin despite its wide margin of safety anything that is overdone becomes dangerous[(1) (2)(3)].

References:

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