Recent Trends in
BIOCHEMISTRY

MEDDOCS
International
Vitamin D in Physiological and Pathological Conditions

Kiran Dahiya*; Sanghapriya Pal; Rakesh Dhankhar
Department of Biochemistry, Pt. BD Sharma PGIMS, Rohtak, Haryana, India.

Abstract
Vitamin D, one of the fat soluble vitamins, is considered a hormone also owing to its ability to be synthesized in the body and similarity of its mechanism of action with steroid hormones. It is the key hormone, along with parathormone and calcitonin, in calcium homeostasis. Besides regulating calcium levels in plasma, vitamin D plays a significant role in maintaining normal physiological functions and growth and development of the body. Deficiency of vitamin D has been implicated in a number of pathological conditions while high levels may produce toxic features. This chapter is an attempt to throw light on these important aspects of vitamin D in human physiology and pathology.

Physiology of vitamin D
Types and sources
Vitamin D derived from the animal sources is in the form of vitamin D₃ (cholecalciferol) and that from plant sources is vitamin D₂ (ergocalciferol). These two are the principal forms of vitamin D. The sources of former include fish oil (saltwater fishes—especially salmon, sardines and herring), liver and egg yolk and that of the latter includes mainly alfalfa, agaricus etc. Over the last several decades, increasing use of sun-block and decreasing exposure to sunlight seen in North America and Western Europe, people’s dependence on food as the source of vitamin D has increased. For this, milk, butter and other dairy products, cereals are being fortified by vitamin D₂ prepared by irradiation of ergosterol from yeast. Vitamin D potency is measured by the...
Recent Trends in Biochemistry

Metabolism of vitamin D

In the Skin

In the skin, a photochemical reaction on exposure to Ultraviolet (UV) component of sunlight causes the formation of cholecalciferol from 7-dehydrocholesterol. The latter is an intermediate in synthesis of the cholesterol. It gets accumulated in the skin. UV rays cause non enzymatic conversion of 7-dehydrocholesterol to previtamin D which, on thermal ionization for period of hours, yields cholecalciferol or calciferol or vitamin D₃, and this gets absorbed in the blood. The production of cholecalciferol in the skin is affected by availability of sunlight. It is decreased by high amount of melanin in the skin and also by the use of high protection sun-blockade, which impairs the penetration of skin by UV rays. The plasma concentration of vitamin D is highest at the end of summer and lowest at the end of winter. The availability of UV fraction of sunlight declines beyond 40° latitude [1].

In the liver

Cholecalciferol, whether produced in the skin or absorbed from the intestine, reaches the circulation where it binds to vitamin D binding protein. Then it reaches the liver where it is hydroxylated at 25-position by acytochrome P450 like enzyme, calcil-25-hydroxylase, in mitochondria and microsomes. It yields 25-hydroxy derivative 25-hydroxycholecalciferol or calcidiol. The latter is released into the circulation. This is the main circulating and storage form of vitamin D. In blood, 88% of it binds to vitamin D binding protein, 0.03% is free and the rest is bound to albumin. Its half-life is 2-3 weeks, which can be reduced in the condition like nephrotic syndrome due to urinary loss of vitamin D binding protein [1].

In the kidney

Next step in the metabolism of vitamin D occurs in the kidney. Here, 25-hydroxyvitamin D-1α hydroxylase causes the secondary hydroxylation to produce 1,25-dihydroxycholecalciferol or calcitriol, the biologically active form of vitamin D. This reaction occurs in the proximal convoluted tubules in the kidney. This enzyme is cytochrome P450 like mixed function oxidase, which is under tight regulation unlike the calcil-25-hydroxylase in the liver. The former is induced by parathormone (PTH) and hypophosphatemia and downregulated by calcium, fibroblast growth factor (FGF23) and 1,25-dihydroxycholecalciferol. This enzyme is also present in different tissues like brain, colon, breast, prostate, beta cells of pancreas, vascular smooth muscle, macrophage and epidermal keratinocyte. But this does not contribute to the circulating level of active form of vitamin D, rather it has paracrine action in those tissues [1].

In kidney there is also another enzyme, vitamin D-24-hydroxylase which hydroxylates at 24th position of 25-hydroxycholecalciferol yielding 24,25-dihydroxycholecalciferol, an inactive metabolite. This is the principal pathway of inactivation of vitamin D, which is present in almost every tissue. Interestingly, 1,25-dihydroxycholecalciferol increases the action of vitamin D-24-hydroxylation leading to inactivation and diminished biological activity of vitamin D. Besides these, there are various polar metabolites of vitamin D, which are secreted in bile and reabsorbed by enterohepatic circulation. So, if the latter is hampered due to any reason like diseases of terminal ileum, it causes the increased loss of vitamin D metabolites [1].

Metabolic role of vitamin D in body

How vitamin D exerts its effects at molecular level

Vitamin D acts through Vitamin D Receptor (VDR), a member of nuclear receptor superfamily. This receptor belongs to a subfamily that also includes the thyroid receptors, retinoid receptors and the peroxisome proliferator-activated receptor. Among these, VDR has only one isoform. From previous discussions, it is evident that vitamin D acts like a steroid hormone and exerts its effects by binding to VDR. The latter binds to Retinoic X Receptors (RXR-which can bind to 9-cis-retinoic acid) and forming a heterodimer, which binds to DNA sequence, stimulates recruitment of necessary molecules and thus initiates the expression of the target gene. The RXRs also form heterodimer with thyroid and other nuclear acting receptors. Deficiency and excess of vitamin A can decrease the action of vitamin D. In deficiency, there is decreased level of 9-cis retinoic acid to form heterodimers, while in excess, there is formation of RXR homodimers what make the RXR receptors unavailable to form heterodimer with VDR. For some target genes, VDR exerts its inhibitory action by interfering the very action of the transcription factors or by recruiting novel proteins to VDR complex. 1,25-dihydroxycholecalciferol has three times more affinity than other vitamin D metabolites and so in physiologic condition the latter do not directly interact with the receptors. But in case of vitamin D toxicity, 25-hydroxycholecalciferol can directly interact with VDR, resulting in hypercalcemia and also can displace 1,25-dihydroxycholecalciferol from vitamin D binding protein leading to rise of its bioavailability [1].

Functions of vitamin D

Role in mineral ion homeostasis

Vitamin D plays an important role in calcium homeostasis. It exerts its effects in three ways:

a) Vitamin D induces the synthesis of calcium binding protein calbindin 9K which is present in the intestinal mucosal cells and is involved in active transport of calcium. Apart from this, there are two major calcium transporter, TRPV5 and TRPV6 (transient receptor potential vanilloid), in the intestinal mucosa, which are also induced by 1,25-dihydroxycholecalciferol. By inducing the expression of these proteins in the intestinal epithelial cells, the latter increases the intestinal absorption of calcium [1].

b) This vitamin is also important for mobilization of calcium from bone. Here, it acts synergistically with PTH. Vitamin D affects osteoblast through its receptor, VDR and increases the expression of different genes encoding bone matrix proteins, osteocalcin and osteopontin and decreases that of type I collagen. Besides this, 1,25-dihydroxycholecalciferol and PTH both induce the synthesis of Receptor Activator of Nuclear Factor K B (RANK) ligand, which binds to RANK present on osteoclast progenitors and mature osteoclasts. This is how they increase the osteoclast differentiation and their activity and thereby bone resorption. Though it was previously thought that 24,25-dihydroxycholecalciferol was an inactive metabolite but recent studies on knock out mouse have showed its ill-defined role in...
bone metabolism [1].

c) 1,25-di hydroxycholecalciferol and PTH together increase
the reabsorption of calcium from distal convoluted tu-
bules of kidney and thereby decreasing the renal excre-
tion of kidney [1].

In these three ways, vitamin D helps to maintain the serum
calcium levels in the body [1].

Role in cell proliferation

Vitamin D is thought to have a regulatory effect on cell pro-
liferation. It has been shown to have anti-proliferative effect
on different cells like keratinocyte, breast cancer cells, prostate
cancer cells [1].

Effect on endocrine system

1,25-di hydroxycholecalciferol acts through VDR receptors
expressed on parathyroid gland and exerts an anti-proliferative
effect and decreases the transcription of PTH, thereby decreasing
its action. This is the background knowledge for strategy to
prevent and treat the hyperparathyroidism in renal insufficiency
[1].

It may have role in secretion of insulin from pancreatic beta
cells and also in synthesis and secretion of thyroid hormone
[1].

Other functions assigned to vitamin D include

a) Regulation of normal functioning of innate and adaptive
system- It has effect in inhibition of production of inter-
leukins by activated T lymphocytes, and of immunoglobu-
lins by activated B lymphocytes and also in differentiation
of monocyte precursor cells [1].

b) Normal functioning of neuromuscular activity[1].

c) Regulation of blood pressure [1].

Pathology associated with vitamin D metabolism

Alteration of vitamin D metabolism can be seen in various
pathological conditions like rickets, osteomalacia, renal dys-
trophy, essential hypertension, multiple sclerosis, rheumatoid
arthritis, different cancers etc. Out of them, few worth mention-
ing disorders have been described here.

Vitamin D deficiency

Vitamin D deficiency is major global public health problem
reported from both sunshine deficient and sunshine sufficient
countries. In spite of this, it is the most underdiagnosed and
untreated nutritional deficiency in the world. Almost 1 bil-
ion people are reported to suffer from vitamin D deficiency
and 50% of the population from vitamin D insufficiency [2]. The
prevalence of vitamin D deficiency is more in elderly and obese
patients and also in hospitalized patients and nursing home
residents. It is 35% higher in obese individual irrespective of
latitude and age [3]. In United States (US), 50% to 60% of hos-
pitalized and nursing home resident patients were reported to
have vitamin D deficiency [4,5]. The condition may be related to
decreased sun exposure resulting from higher skin content of
melanin and also the practice of higher skin coverage especially
in Middle Eastern countries. In United States, 47% of African
American infants and 56% of Caucasian infants, while 90% of in-
fants in Iran, Turkey and India have vitamin D deficiency. Among
the adults, it has been observed that 35% in US have vitamin
d deficiency, on the other hand, in India, Pakistan and Bangla-
desh more than 80% are vitamin D deficient. When it comes to
elderly population (>60 years), 61% in US, 90% in Turkey, 96%
in India, 72% in Pakistan and 67% in Iran are vitamin D deficient
[6].

Causes of vitamin D deficiency

The deficiency of vitamin D mainly results from decreased
production in skin, lack of dietary intake, increased loss, im-
paired vitamin D activation and resistance to biologic action of
1,25-di hydroxycholecalciferol.

a) Vitamin D deficiency due to decreased production or in-
take:

1) In case of aged and hospitalized patients, there is reduced
exposure to sunlight as well as reduced absorption in intes-
tine with age, leading to deficiency.

2) Reduced intake through diet may be a cause in various
populations.

3) Intestinal malabsorption, particularly of dietary fats, spe-
cially in terminal ileal disease where there is decreased
enterohepatic circulation of vitamin D metabolites result-
ing in increased loss of those compounds.

b) Increased loss of vitamin D:

1) Due to increased catabolism resulting from induction of
hepatic cytochrome P-450 by various drugs like barbitu-
rates, phenytoin, rifampin.

2) Decreased enterohepatic circulation leading to increased
loss of vitamin D metabolites.

3) Nephrotic syndrome

c) Decreased 25-hydroxylation:

1) In severe liver disease

2) Use of isoniazid

d) Reduced 1α hydroxylation:

1) Renal failure

2) 1α hydroxylase mutation like in genetic disorder pseudovi-
tamin D deficiency.

3) Hypoparathyroidism

4) Oncogenic osteomalacia

5) X-linked hypophosphatemic rickets

6) Use of ketoconazole

e) Resistance in the target organ :

Mutation in the vitamin D receptor like hereditary vitamin D
resistant rickets which is more difficult to treat [7].

Clinical features

The clinical features mainly result from the impaired calcium
absorption. Mild to moderate deficiency may be asymptomatic
but longstanding one may be manifested with secondary hyper-
parathyroidism, impaired mineralization of bone characterized
by osteopenia on X-ray and proximal myopathy. The latter rarely
may show the features of acute hypocalcemia as numbness tin-
gling seizures [7].
**Rickets and osteomalacia**

Vitamin D is manifested as rickets in children before epiphyseal fusion. There is continued formation of osteoid matrix and cartilage but there is improper mineralization of it resulting in soft, pliable bones, growth retardation with expansion of growth plate. In normal cases, three layers of chondrocytes are present in growth plate: the reserve zone, the proliferative zone, and hypertrophic zone. Rickets is characterized by expansion of hypertrophic layer as the result of impaired apoptosis of late hypertrophic chondrocytes. Moreover, in murine models, it is seen that hypophosphatemia is important etiologic factor for the development of rachitic growth plate. [8] Clinical features include:

1) Craniotabes: In this feature, pressure over soft membranous skull bone will give feeling of ping-pong ball being compressed.
2) Bossing of the skull: Bossing of frontal and parietal bone, mainly seen after 6 months of age.
3) Broadening of the end of the long bones, mainly around wrists and knees, seen about 6-9 months of age.
4) Delayed teeth eruption.
5) Harrison's sulcus: Horizontal depression along the lower part of chest corresponding to insertion of the diaphragm.
6) Pigeon chest: Sternum is prominent.
7) Rachitic rosy: The costo-chondral junctions of anterior chest wall become prominent.
8) Muscular hypotonia: The child's abdomen is protruberant (pot belly), and viscerotopsis and lumbar lordosis are also seen.
9) Deformities: A variety of deformities like knock knees or bowed legs which become evident as the child starts to walk [9].

Osteomalacia occurs due to vitamin D deficiency in adults resulting in demineralization of preexisting bone leading to more susceptibility to fracture. Unlike osteoporosis, osteoid matrix remains intact here. It may be a feature of long-standing hypophosphatemia due to either renal phosphate wasting or chronic use of etidronate or phosphate-binding antacid. [8] Clinical features include:

1) Bone pains: It may range from skeletal discomfort to diffuse pain, even tenderness is common.
2) Muscular weakness: Difficulty in climbing up and down stairs. Waddling gait may be seen. Tetany may manifest at carpopedal spasm and facial twitching.
3) Spontaneous fracture: Mainly in spine leading to kyphosis [9].

**Diagnosis of vitamin D deficiency, rickets and osteomalacia**

1) The most specific screening test for vitamin deficiency is estimation of serum 25-hydroxycholecalciferol. The different criteria are stated in Table 1 [10].

<table>
<thead>
<tr>
<th>Condition</th>
<th>Serum levels of 25-(OH) vitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sufficiency</td>
<td>More than or equal to 30 ng/mL</td>
</tr>
<tr>
<td>Relative Insufficiency</td>
<td>21-29 ng/mL</td>
</tr>
<tr>
<td>Deficiency</td>
<td>Less than or equal to 20 ng/mL</td>
</tr>
<tr>
<td>Toxicity</td>
<td>&gt;150 ng/mL</td>
</tr>
</tbody>
</table>

2) There may be decreased serum total and ionized calcium [8].

3) Due to PTH induced bone turn over there may be increased alkaline phosphatase. It is also associated with phosphaturia and hypophosphatemia as PTH induces the urinary calcium retention and phosphate excretion [8].

4) As PTH is an important stimulus for renal 1α hydroxylase, paradoxically level of 1,25-dihydroxycholecalciferol may be increased some times. This is the reason why the latter does not reflect the status of vitamin D in body and should not be used to diagnose the vitamin D deficiency [8].

5) **Radiologic findings:**

For rickets: Delayed appearances of epiphysis, widening of epiphyseal plate, cupping and splaying of metaphysis, bone deformities and in late cases rarefaction of diaphyseal cortex [9].

For osteomalacia: Diffuse rarefaction of bones, looser's zone or pseudo fracture (radiolucent zone at sites of stress; common sites include pubic rami, auxiliary border of scapula, ribs, the medial cortex of the neck of femur; it is due to rapid resorption and slow mineralization and the zone may be surrounded by collar of callus), triradiate pelvis in females, protrusio-acetabuli (protruding acetabulum into pelvis) [9].

**Treatment of vitamin D deficiency**

The condition is treated with vitamin D supplementation. Based on observation that 400IU supplementation is often insufficient to prevent deficiency, and 800IU along with calcium supplementation reduces the risk of hip fractures in elderly women, the high doses are preferred. Vitamin D should always be supplemented along with calcium because most of the features of deficiency are due to hypocalcemia. Toxicity occurs with the dose 40000IU daily. Patients having impaired 1α-hydroxylation, are treated by metabolites not requiring this activation step like 1,25-dihydroxyvitaminD3 (calcitriol,0.25-0.5 μg/d) and 1α-hydroxyvitaminD2 (hecotrol,2.5-5μg/d). Severe deficiency is treated by initially 50000IU weekly for 3-12 weeks, followed by 8000IU daily. Calcium supplementation should be 1.5-2 g/d of elemental calcium [8].

In response to treatment, normocalcemia occurs within one week, though, increased PTH and alkaline phosphatase levels persist for 3-6 months. Treatment monitoring is done by measuring serum and urinary calcium. If the treatment is adequate then, 24-hour urinary calcium excretion will be in the range of 100-250mg/24-hours, if less, it means any problem regarding patient’s compliance to treatment regimen or absorption of calcium or vitamin D supplement. The levels of >250mg/24-
hours are associated with nephrolithiasis requiring a reduction of doses [8].

**Vitamin D toxicity**

The increased level of plasma concentration leads to toxicity characterized by contraction of blood vessels, resulting in increased blood pressure and calcification i.e. deposition of calcium in the soft tissues. With increased level of vitamin D, there will also be increased bone resorption and calcium absorption resulting in hypercalcemia and hypercalciuria, and the latter will increase the predisposition of renal stone formation. Some infants may be sensitive to dose of vitamin D as low as 50 μg/day. Toxicity is seen in excessive dietary intake but not in excessive exposure to sunlight. It is because that our body has limited capacity to synthesize precursor, 7-dehydrocholesterol and excessive exposure results in formation of inactive metabolites [10].

**Vitamin D and other diseases**

Besides playing a crucial role in calcium homeostasis, vitamin D exerts a variety of functions in the body. On account of this fact, altered levels of vitamin D have been found to be associated with a number of clinical disorders. A few of them have been discussed here in a bit detail:

**Renal osteodystrophy**

One of the complications of the chronic renal failure is renal osteodystrophy. There is inability of body to produce 1,25-dihydroxychocolcalciferol and so the bone calcium becomes the source to maintain the serum level. Besides, the condition is associated with renal retention of phosphate and hyperphosphatemia. This leads to formation of calcium phosphate resulting in deposition of the latter in soft tissues, metastatic calcification, reducing the level of calcium further. Thus the combination of hypocalcemia and hypophosphatemia increases the secretion of parathyroid hormones resulting in bone resorption. Therefore, in this case treatment with only vitamin D or its metabolites will not help because it will rather increase metastatic calcification due to hypercalcemia resulting from the treatment and already existing hypophosphatemia. So, important is to reduce the phosphate level alongside the high calcium diets/vitamin D supplements. As it is difficult to reduce phosphate component in diet, vegetable proteins are preferred over animal ones, for, in them phosphates are in the form of phytates which are not readily absorbed. The patients are also asked to avoid processed food as phosphates are added to them. For all the above reasons, phosphate binders are used. They are calcium acetate and cationic polymer called sevalamer hydrochloride. If orally administered 1,25-dihydroxyvitamin D is not sufficient to raise serum calcium level, as in severe hyperparathyroidism, intravenous form may be given. Lot of research is going on to develop calcimimetic agents which can bind to calcium sensor on the parathyroid gland, thereby decreasing its secretion [11].

**Cystic fibrosis**

This is the disease caused by the mutation of the gene encoding Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), a cAMP regulated chloride channel. It is the most common lethal inherited disease among Caucasians. This defect leads to problem in the activity of exocrine glands affecting mainly the lungs and the pancreas. In the lungs, there is viscid secretion in bronchi and bronchioles blocking the lumen and it also results in frequent infections. On the other hand, dysfunction of exocrine cells of pancreas results in deficiency of pancreatic enzymes and also partial obstruction of common bile duct. Consequently, deficiency of pancreatic amylase, proteases and lipase will lead to severe malabsorption. Due to fat malabsorption resulting from lipase and bile deficiency, there will be associated fat soluble vitamin deficiency. Calcium binds with long chain fatty acids to form insoluble salts. Partially digested food bolus too hinders the absorption of starch and proteins by physical entrapment of those molecules. Besides these, increased mucus secretion in the intestinal lumen also reduces the absorption of several micronutrients like iron [11].

Patients are treated with preparation of pancreatic enzymes. Although, with this, the absorption of protein and carbohydrates approximates to normal, that of fat does not. It is due to the fact that there remains the persistent deficiency of bile acid and excessive mucus secretion. Moreover, for some patients calorie demand is increased due to chronic infection. The recommendation is high energy, high protein diet without restriction of dietary fats (50% carbohydrate, 15% protein, 35% fat). If diet fails to supply the need of the body, then supplementary feed or enteral feeding comes into the picture. Sometimes, medium chain fatty acids may be advised because they get absorbed directly in the intestinal mucosa. Children of age 2-8 years are treated with multivitamin preparation containing 400IU of vitamin D and 5000IU of vitamin A, though, older children, adolescent and adults need 1-2 dose per day. Vitamin K is only recommended when patient is on antibiotics or suffering from cholestatic liver disease. In spite of the fact that iron deficiency is commonly associated with this condition, it is not recommended because of chance of high level of iron to enhance probability of systemic bacterial infection. Although calcium level is normal in these patients, it is noteworthy to maintain its recommended level in diet [11].

**Vitamin D and cancer**

Alteration of vitamin D level has been implicated in the risk and progression of various cancers. Different research works have supported this fact. It goes long back to 1915 when Hoffman first noticed the association of sun exposure and latitude with cancer mortality. Peller and Stephenson found that people who were exposed to sunlight sufficient to induce nonlethal, non-melanoma skin cancer, had lower incidence of more malignant tumors. In 1980s to 90s, Garland et al and Gorham et al conducted a number of epidemiologic studies and concluded that there was a strong negative correlation between latitude, sun exposure and poor vitamin D status and the risk of developing many deadly cancers like that of colon, breast, ovarian and melanoma. Age adjusted death rates among the patients of colon cancer have been found to be high in areas with low levels of winter sunlight. A study showed that the individuals with 25-hydroxyvitamin D level <30ng/mL had higher incidence of colonic adenomas. The association of 25-hydroxyvitamin D with risk of colon cancer was present both early and late in follow-up, suggesting that vitamin D metabolites may have effects at all stages of carcinogenesis. There are 7 epidemiological studies indicating the higher risk of colon cancer in individuals taking lower amounts of vitamin D including Western Electric Cohort Study, the Nurses’ Health Study, the Male Health Professionals’ Follow-Up Study, the Iowa Women’s Health Study, and the American Cancer Society Cancer Prevention Study II (CPS II) Cohort Study and 2 case control study. There are also studies reporting that breast cancer death rates are higher in areas with low winter sunlight levels. Women who are exposed to sufficient sunlight on regular basis, seem to have significantly lower
incidence of breast cancer. Low levels of 25-hydroxy vitamin D may be attributed to faster progression of breast cancer. Moreover, mortality rates of perimenopausal ovarian cancer have also been found lower in sunny regions. The same effect can be seen in case of prostate cancer. In a study of 19000 men, those with levels of 25-hydroxyvitamin D <16ng/mL had a higher incidence of prostate cancer than those having more than this value. Although, there are few studies showing no association between vitamin D and cancer, making the topic controversial [12,13].

We know that vitamin D is involved in regulation of cellular proliferation and maturation. Nevertheless, the exact mechanism is not fully understood. A number of genes controlling proliferation, differentiation, apoptosis and angiogenesis, are directly or indirectly affected by vitamin D. The active form of the latter increases inhibitors and decreased activators of cyclin-cyclin dependent kinase complexes in addition to increasing levels of cyclin dependent kinase inhibitors Cip/Kip proteins P21 and P27. These proteins are known to keep the cell cycle in the G1/S phase, preventing DNA synthesis and so, the cell proliferation [12].

Vitamin D and autoimmune diseases

Vitamin D is known to have important immunomodulatory effects in body. Dendritic cells are primary targets for this activity of 1,25-dihydroxycholecalciferol, the active form of vitamin D. It is indicated by inhibited dendritic cells differentiation and maturation leading to down regulated expression of MHC-II, co-stimulatory molecules like CD40, CD80, CD86 and decreased production of IL-12. Besides these, 1,25-dihydroxycholecalciferol increases IL-10 production and thereby, promotes dendritic cell apoptosis. In this way, vitamin D inhibits dendritic cell dependent T-cell activation. Apart from these, vitamin D receptor agonists seem to inhibit pathogenic pro-inflammatory T-cells like Th1 and Th17 and under appropriate conditions they tend to favor a deviation to Th2 pathway [14].

These types of immunomodulatory and anti-inflammatory effects are particularly efficient for the rheumatoid arthritis patients to support a therapeutic role of 1,25-dihydroxycholecalciferol in this disease. From different studies, it is also seen that vitamin D may play an important role in maintenance of B-cell homeostasis and correction of vitamin D deficient state may affect the treatment of B-cell mediated autoimmune disorders such as systemic lupus erythematosus (SLE) [14].

Conclusion

It is obvious from the above discussion that vitamin D is important in the body to maintain physiologic homeostasis. Besides this, alteration of vitamin D status in the body, underlies different pathologic conditions. Therefore, vitamin D is gaining great interest in recent biomedical research works.

References