# A Survey on Awareness of Calcium and Vitamin D among Women in Dhaka City

**A Dissertation submitted to the Department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the Requirements for the Degree of Bachelor of Pharmacy**


**Submitted by**

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# Declaration by the Research Candidate

I, **AynanTajriya, ID: 2012-3-70-015**, hereby declare that the dissertation entitled— **Awareness of Calcium and Vitamin D among women in Dhaka City**. Submitted by me to the **Department of Pharmacy, East West University** in partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy is a record of research work under the supervision and guidance of **Farah Shahjin**, Senior Lecturer, Department of Pharmacy, East West University, Dhaka.

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## Certificate by the Supervisor

This is to certify that the thesis entitled "**Awareness of Calcium and Vitamin D among women in Dhaka City**" submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bonafide record of original and genuine research work carried out by **AynanTajriya, ID: 2012-3-70-015** in 2016 of her research in the Department of Pharmacy, East West University, under the supervision and guidance of me.

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# Certificate by the Chairperson

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## Dedication

This research work is dedicated to my beloved parents,
Honorable faculties and loving friends.

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## Abbreviation

- g- gram
- m/mol-mili mole
- ca- Calcium
- EDTA- Ethylenediaminetetraacetic acid
- FDA- Food and Drug Adminstration
- DXR-X ray radiogrammetry
- dL- Desi Litre
- PTH-Para thyroid hormone
- 25-OHD- Calcitriol
- Vit D2-Ergocalcitriol

**Abstract**

Calcium is essential to maintaining total body health, normal growth and development, metabolizing iron, helping blood clotting & regulating blood pressure, keeping bones & teeth strong over lifetime, the action of the number of hormones, cell structure etc. Vitamin D is required for regulation of cell growth, bone formation, immune function, muscle strength, hair growth, reducing autoimmune disease, fighting infection etc. Majority of the women have not been prescribed calcium supplement for bone disorder. Lack of awareness and insufficient knowledge of the essentiality of these two nutrients are assumed to cause this problem in Bangladesh. The present study was designed and conducted to establish a basic understanding on the level of gap of knowledge and awareness among college going students in Bangladesh. Bangladesh is a one of the most overpopulated country of the world. That's why the most important part in living is to be as healthy as possible avoiding all the diseases. From the survey it was found that about the 75% & 80% women know Calcium & Vitamin D as a food supplement while 25% & 20% do not know about the Calcium & Vitamin D. The term of "Osteoporosis" are known (32%) of women while (78%) & do not know about it. (38%) and (40%) ever been prescribed any Calcium & Vitamin D supplement by a physician while (65%) and (60 %) ever not been prescribed. The women have come to highly know about Calcium and Vitamin D from those source as books (65%).

**Key words: Calcium, Vitamin D, Calcitriol, Cholecalciferol, awareness.**

# Chapter one
# Introduction

# Introduction

## 1.1 Overview

Calcium and vitamin D are two important micronutrients for maintaining proper bone health. They play a key role in preventing as well as treating different clinical conditions with excessive bone loss. They are considered to be essential for increasing peak bone mass and for minimizing age-related bone loss to reduce the risk of osteoporosis and low-trauma fractures. It is evident that vitamin D is one of the 13 essential dietary vitamins and is important for intestinal absorption of calcium. Apart from its skeletal effect, vitamin D is associated with reduction of the risk of cancer, autoimmune, infectious and cardiovascular diseases. Vitamin D and calcium both can be obtained directly from regular diet and supplementation. The dietary source of calcium is relatively common than that of vitamin D. Vitamin D is synthesized in our body after exposure to sunlight. But this exposure is sometimes compromised due to increased tendency to avoid sunlight exposure for cosmetic or cultural reasons and concerns about the potential risk of skin cancer.

Numerous reports have shown that relatively high proportions of people have inadequate levels of vitamin D. The extracellular health benefits of vitamin D and high prevalence of inadequate levels of vitamin D have been largely unrecognized by both physicians and patients. A survey conducted by International Osteoporosis Foundation in 2007 reported that while patients are knowledgeable about the role of calcium as a bone building agent, but they are less concerned about the role of vitamin D in this process. Data are available from studies on young adults, elderly persons; including elderly women, post-menopausal women who are at highest risk of developing osteoporosis and healthy adolescents from different countries. Some studies have also shown the prevalence of calcium and vitamin D insufficiency and the related consequences in respect to Bangladesh. More recently, studies carried across different countries in South and Southeast Asia have found that, with few exceptions, widespread prevalence of hypovitaminosis D in both male and female and all age groups of the population. Calcium deficiency rickets has been described in children from a number of countries including Bangladesh. In the Indian subcontinent, rickets in

infants, older children and adolescents has been reported in India, Bangladesh and Pakistan. Among the underlying causes of these diseases, maternal vitamin D deficiency and low dietary calcium were important. Another two studies also reported significant prevalence of rickets in children in Bangladesh due to dietary calcium insufficiency.

There is a gap of knowledge regarding the essentiality of calcium and vitamin D among people in Bangladesh. This gap should be minimized by understanding the extent and magnitude of the problem. Bangladesh is a developing country in South Asia with a burden of large population. The people here lack the basic needs along with the need of proper healthcare. Health education system along with healthcare system is not sufficient to meet all the public health related demands in this country. A vast majority of people lack proper education, they do not know sufficient about improving their health. It is assumed that people in Bangladesh are not conscious or aware of the importance of calcium and vitamin D for proper bone health. The university going students are at the top level of their education who are believed to have some short of knowledge regarding the significance of calcium and vitamin D. The current study was designed to get an idea about the degree of shortage of knowledge regarding the use of calcium and vitamin D among the university going educated population which would help us to make an assumption about the knowledge gap exists among the general people and to take appropriate steps to fill it up.(Uddin, Riaz et al. 2013)

### 1.2 Physiology and pharmacology of Calcium

Calcium is the major extracellular divalent cation. The normal adult man and women posses about 1300 and 1000 gm of Calcium of which more than 99% in bone. Calcium is present in small amount in extracellular fluids and to a minor extent within the cell (Goodman and Gillman, 2002). Calcium accounts for 1 to 2 percent of adult human body weight. Over 99 percent of total body calcium is found in teeth and bones. The remainder is present in blood, extracellular fluid, muscle, and other tissues, where it plays a role in mediating vascular contraction and vasodilation, muscle contraction, nerve transmission, and glandular secretion. In bone, calcium exists primarily in the form of hydroxyapatite and bone mineral is almost 40 percent of the weight of bone.

Bone is a dynamic tissue that is constantly undergoing osteoclastic bone resorption and osteoblastic bone formation. Bone formation exceeds resorption in growing children, is balanced with resorption in healthy adults, and lags behind resorption after menopause and with aging in men and women. Each year, a portion of the skeleton is remodeled (reabsorbed and replaced by new bone). The rate of cortical (or compact) bone remodeling can be as high as 50 percent per year in young children and is about 5 percent per year in adults (Parfitt, 1988). Trabecular (or cancellous) bone emodeling is about five-fold higher than cortical remodeling in adults. The skeleton has an obvious structural role and it also serves as a reservoir for calcium. The skeleton contains 99% of total body calcium in a crystalline form. The steady state content of calcium in bone reflects the net effect of bone resorption and bone formation. In addition, a liable pool of bone calcium is readily exchangeable with intestinal fluid. The rate of exchanges are modulated by drug, hormone, vitamin and other factor that directly alter bone turnover or that influence the level of Calcium in intestinal fluid (Goodman and Gillman, 2002).Awareness of Calcium & Vitamin D among college going students in Bangladesh.

**Table: 1.1- Calcium recommended for women and children**

| Age | Dietary Allowance (IU/day) | Dietary Allowance (mg/day) |
|---|---|---|
| 1 - 3 years old | 700 | |
| 4 - 8 years old | 1000 | 600 |
| 9 - 13 years old | 1300 | 600 |
| 14 - 18 years old | 1300 | 600 |
| 19 - 30 years old | 1000 | 600 |
| 31 - 50 years old | 1000 | 600 |
| 51 - 70 years old | 1200 | 600 |
| 51 - 70 year old females | 1200 | 600 |
| 71+ years old | 1200 | 800 |
| 14 - 18 years old, pregnant/ lactating | 1300 | 600 |
| 19 - 50 years old, pregnant/lactating | 1000 | 600 |

*For infants, adequate intake is 200 mg/day for 0 to 6 months of age and 260 mg/day for 6 to 12 months of age.

**For infants, adequate intake is 400 IU/day for 0 to 6 months of age and 400 IU/day for 6 to 12 months of age.*(Nlm.nih.gov*, 2016)

### 1.3 Sources of Calcium

There are many foods to choose from that provide calcium. Milk and milk products—such as low-fat or fat-free cheese and yogurt—are excellent sources because they are high in calcium. Most types of milk have approximately 300 milligrams of calcium per 8 fluid ounces (1 cup), or about 25 percent of the calcium that twins and teens need every day. The best choices are low fat or fat-free milk and milk products. Because these items contain little or no fat, it's easy to get enough calcium without adding extra fat to the diet. Flavored milk has just as much calcium as plain milk, but is higher in sugar and calories than plain milk. Young people may choose to drink chocolate or other flavored milk if they prefer the taste, but they should remember to factor in the additional calories into their overall daily needs. Whether plain or flavored, remember to choose low-fat or fat-free milk and milk products. For those individuals who do not consume adequate amount of milk or dairy products, a supplement may be necessary. (Autajay, 2003).

### 1.4 Physiological role of calcium

#### 1.4.1 Participates in the structure of bones and teeth-

At least 99% of the total amount of calcium is in the bones and teeth. Calcium in the bones is transformed into a hydroxyapatite but the bones also contain significant amounts of calcium phosphate, carbonate, citrate, fluoride, magnesium, strontium, trace and minor amounts of other salts. Minerals account about 50% of the total bone mass. The rest is organic matrix in which are proteins, glycoproteins and proteoglycans that bind calcium salts. Every day in the bones can be exchanged up to 700 mg of calcium. The immediate source of calcium for bones is calcium from the body fluids and cells. Although the this amount of calcium is small (<10 g) compared to the amount of bone it is critically important for the regulation surprisingly large number of cellular activities.

### 1.4.2 Metabolic regulation in human body

This is one of the main roles of calcium. Protein kinases, which modulate the activity of key enzymes as a response to hormone binding to the surface of cells, are calcium activated - either directly, or binding to a protein that binds calcium - calmodulin.

### 1.4.3 Regulation of cellular activity in human body

These include nerve and muscle function, hormone action, blood coagulation, cell motility, and many others. Regulates muscle contraction by regulating the contractility of actin and myosin. Since it participates in such a large number of cellular regulation it is also called the "second messenger".

The way of this action is analogous to the regulatory actions of cyclic nucleotides. Effects of calcium are mediated by an intracellular receptor protein - calmodulin, which binds calcium ions when their concentration in the reaction to the stimulus increases. Calmodulin has been found in every studied cell that contains the nucleus. When Calcium binds to calmodulin it activity many enzymes, and among them are those who participate in the metabolism of cyclic nucleotides, protein phosphorylation, secretory function, muscle contraction, the formation of microtubules, glycogen metabolism and calcium flux. It were found that potent inhibitors of calmodulin activity are phenothiazine drugs that relax the smooth muscles of several peptides that are found in poisonous insects.

### 1.4.4 Part of many metalloenzyme

For example. α-amylase and phospholipase contain calcium as an essential part of the catalytic. Osteocalcin is a protein from the bones which is important for normal bone mineral crystallization. Calbindin D is essential for intestinal absorption of calcium, the translation of calcium into the cells and the absorption of calcium from the glomerular filtrate in the kidney. Some of the blood proteins must bind calcium for their activity. Many anticoagulants bind calcium chelate structures (such as EDTA and citrate).

### 1.5 Calcium-binding proteins calcium effect

#### 1.5.1 Secretion of hormones and neurotransmitters

Annexin protein must bind to calcium tu bind to a phospholipid membrane. On this case it initiate cellular secretory vesicles to fuse with the surface of membrane and then exocytosis.

#### 1.5.2 Cell adhesion.

Kaderine are calcium-dependent proteins that regulate cell adhesion and normal contact inhibition of cell replication. Defect in the function of kaderine is linked to the development of malignancy.

#### 1.5.3 Cytoskeleton proteins.

The importance of Calcium in these activities is reflected in the precision which regulates the concentration of Calcium concentrations. Normal plasma contains 9-11 mg of calcium per 100 mL. Daily variations are rarely greater than ±3%. These narrow limits reflect the complex regulatory action of vitamin D, parathyroid hormone, calcitonin and other hormones.*(Mineravita*, 2016)

### 1.6 Calcium metabolism in human body

Calcium metabolism refers to all the movements (and how they are regulated) of calcium atoms and ions into and out of various body compartments, such as the gut, the blood plasma, the interstitial fluids which bathe the cells in the body, the intracellular fluids, and bone. An important aspect, or component, of calcium metabolism is plasma calcium homeostasis, which describes the mechanisms whereby the concentration of calcium ions in the blood plasma is kept within very narrow limits.Derangements of this mechanism lead to hypercalcemia or hypocalcemia, both of which can have important consequences for health. In humans, when the blood plasma ionized calcium level rises above its set point, the thyroid gland releases calcitonin, causing the plasma ionized calcium level to return to normal. When it falls below that set point, the parathyroid glands release parathyroid hormone causing the plasma calcium level to rise.

### 1.6.1 Calcium concentrations in human body

Calcium is the most abundant mineral in the human body. The average adult body contains in total approximately 1 kg, 99% in the skeleton in the form of calcium phosphate salts. The extracellular fluid contains approximately 22 mmol, of which about 9 mmol is in the plasmaApproximately 10 mmol of calcium is exchanged between bone and the ECF over a period of twenty-four hours.The concentration of calcium ions inside the cells (in the intracellular fluid) is more than 7,000 times lower than in the blood plasma (i.e. at <0.0002 mmol/L, compared with 1.4 mmol/L in the plasma).

### 1.6.2 Absorption of calcium from the intestine in human body

The normal adult diet contains about 25 mmol of calcium per day. Only about 5 mmol of this is absorbed into the body per day.

Calcium is absorbed across the intestinal epithelial cell's brush border membrane and is immediately bound to calbindin, a vitamin D-dependent calcium-binding protein. Calbindin transfers the calcium directly into the epithelial cell's endoplasmic reticulum, through which the calcium is transferred to the basal membrane on the opposite side of the cell, without entering its cytosol. From there TRPV6 and calcium pumps actively transport calcium into the body. Active transport of calcium occurs primarily in the duodenum portion of the intestine when calcium intake is low; and through passive paracellular transport in the jejunum and ileum parts when calcium intake is high, independently of Vitamin D level.

The active absorption of calcium from the gut is regulated by the calcitriol (or 1,25 dihydroxycholecalciferol, or 1,25 dihydroxyvitamin D3) concentration in the blood. Calcitriol is a cholesterol derivative. Under the influence of ultraviolet light on the skin, cholesterol is converted to previtamin D3 which spontaneously isomerizes to vitamin D3 (or cholecaliferol). Under the influence of parathyroid hormone, the kidneys convert cholecalciferol into the active hormone, 1,25 dihydroxycholecalciferol, which acts on the epithelial cells (enterocytes) lining the small intestine to increase the rate of absorption of calcium from the intestinal contents. Low parathyroid hormone levels in the blood (which occur under physiological conditions when the plasma ionized calcium levels are

high) inhibit the conversion of cholecalciferol into calcitriol, which in turn inhibits calcium absorption from the gut. The opposite happens when the plasma ionized calcium levels are low: parathyroid hormone is secreted into the blood and the kidneys convert more cholecalciferol into the active calcitriol, increasing calcium absorption from the gut. Since about 15 mmol of calcium is excreted into the intestine via the bile per day, the total amount of calcium that reaches the duodenum and jejunum each day is about 40 mmol (25 mmol from the diet plus 15 mmol from the bile), of which, on average, 20 mmol is absorbed (back) into the blood. The net result is that about 5 mmol more calcium is absorbed from the gut than is excreted into it via the bile. If there is no active bone building (as in childhood), or increased need for calcium during pregnancy and lactation, the 5 mmol calcium that is absorbed from the gut makes up for urinary losses that are only partially regulated. Most excretion of excess calcium is via the bile and feces, because the plasma calcitriol levels (which ultimately depend on the plasma calcium levels) regulate how much of the biliary calcium is reabsorbed from the intestinal contents. Urinary excretion of calcium is relatively modest (about 5 mmol/day) in comparison to what can be excreted via the feces (15 mmol/day).

Not all the calcium in the diet can be readily absorbed from the gut. The calcium that is most readily absorbed is found in dairy product and eggs, as well as in tinned fish products. The calcium contained in vegetable matter is often complexed with phytates, oxalates, citrate and other organic acids, such as the long-chained fatty acids (e.g. palmitic acid), with which calcium binds to form insoluble calcium soaps.

### 1.6.3 Excretion of calcium through kidneys

The kidney filters 250 mmol of calcium ions a day in pro-urine (or glomerular filtrate), and resorbs 245 mmol, leading to a net average loss in the urine of about 5 mmol/d. The quantity of calcium ions excreted in the urine per day is partially under the influence of the plasma parathyroid hormone level - high levels of parathyroid hormone decreasing the rate of calcium ion excretion, and low levels increasing it. However, parathyroid hormone has a greater effect on the quantity of phosphate ions excreted in the urine. Phosphates form insoluble salts in combination with calcium ions. High concentrations of hydrogen phosphate in the plasma, therefore, lower the ionized

calcium level in the extra-cellular fluids. Thus, the excretion of more phosphate than calcium ions in the urine raises the plasma ionized calcium level, even though the total calcium concentration might be lowered. The kidney influences the plasma ionized calcium concentration in yet another manner. It processes vitamin D3 into calcitriol, the active form that is most effective in promoting the intestinal absorption of calcium. This conversion of vitamin D3 into calcitriol, is also promoted by high plasma parathyroid hormone levels.

### 1.7 The role of calcium in bone

Although calcium flow to and from the bone is neutral, about 5–10 mmol is turned over a day. Bone serves as an important storage point for calcium, as it contains 99% of the total body calcium. Calcium release from bone is regulated by parathyroid hormone in conjunction with calcitriol manufactured in the kidney under the influence of parathyroid hormone. Calcitonin (a hormone secreted by the thyroid gland when plasma ionized calcium levels are high or rising; not to be confused with "calcitriol" which is manufactured in the kidney) stimulates incorporation of calcium into bone.

A low calcium intake may be a risk factor in the development of osteoporosis in later life. In one meta-analysis, the authors found that in fifty out of the fifty-two studies that they reviewed, a diet adequately rich in calcium reduced calcium loss from bone with advancing (post-menopausal) age. A diet with sustained adequate amounts of calcium reduced the risk of osteoporosis.

### 1.8 Regulation of calcium metabolism

A diagrammatic representation of the movements of calcium ions into and out of the blood plasma in an adult in calcium balance. The widths of the arrows indicating movement into and out of the plasma are roughly in proportion to the daily amounts of calcium moved in the indicated directions. The size of the central square in not in proportion to the size of the diagrammatic bone, which represents the calcium present in the skeleton, and contains approximately 25,000 mmol (or 1 kg) of calcium compared to the 9 mmol (360 mg) dissolved in the blood plasma. The various colored arrows indicate where the different hormones act, and their effects when their plasma levels are

high. In parathyroid hormone, calcitriol dihydroxyvitamin D3, and calcitonin is a hormone secreted by the thyroid gland when the plasma ionized calcium level is high or rising. The diagram does not show the extremely small amounts of calcium that move into and out of the cells of the body, nor does it indicate the calcium that is bound to the extracellular proteins or to plasma phosphate.

The plasma ionized calcium concentration is regulated to within very narrow limits (1.3–1.5 mmol/L), despite being the central hub through which calcium is moved from one body compartment to the other (see diagram on the right). This is achieved by both the parafollicular cells of the thyroid gland, and the parathyroid glands constantly sensing (i.e. measuring) the concentration of calcium ions in the blood flowing through them. When the concentration rises the parafollicular cells of the thyroid gland increase their secretion of calcitonin (a proteinaceous hormone) into the blood. At the same time the parathyroid glands reduce their rate of parathyroid hormone secretion into the blood. The resulting high levels of calcitonin in the blood stimulate the skeleton to remove calcium from the blood plasma, and deposit it as bone. The reduced levels of parathyroid hormone inhibit removal of calcium from the skeleton. The low levels of parathyroid hormone have several other effects: they increase the loss of calcium in the urine, but more importantly inhibit the loss of phosphate ions via that route. Phosphate ions will therefore be retained in the plasma where they form insoluble salts with calcium ions, thereby removing them from the ionized calcium pool in the blood. The low levels of parathyroid hormone also inhibit the formation of calcitriol from cholecalciferol (vitamin D3) by the kidneys. The reduction in the blood calcitriol concentration acts (comparatively slowly) on the epithelial cells (enterocytes) of the duodenum inhibiting their ability to absorb calcium from the intestinal contents. The low calcitriol levels also act on bone causing the osteoclasts to release less calcium ions into the blood plasma.

When the plasma ionized calcium level is low or falls the opposite happens. Calcitonin secretion is inhibited and parathyroid hormone secretion is stimulated, resulting in calcium being removed from bone to rapidly correct the plasma calcium level. The high plasma parathyroid hormone levels inhibit calcium loss via the urine while stimulating

the excretion of phosphate ions via that route. They also stimulate the kidneys to manufacture calcitrol (a steroid hormone), which enhances the ability of the cells lining the gut to absorb calcium from the intestinal contents into the blood, by stimulating the production of calbindin in these cells. The parathyroid hormone stimulated production of calcitriol also causes calcium to be released from bone into the blood, by the release of a cytokine, or local hormone from the osteoblasts which increases the bone resorptive activity by the osteoclasts. These are, however, a relatively slow processes.

Thus fast short term regulation of the plasma ionized calcium level primarily involves rapid movements of calcium into or out of the skeleton. Longer term regulation is achieved by regulating the amount of calcium absorbed from the gut or lost via the feces.

### 1.9 Pathology of calcium

Hypocalcemia and hypercalcemia are both serious medical disorders.Renal osteodystrophy is a consequence of chronic renal failure related to the calcium metabolism.Osteoporosis and osteomalacia have been linked to calcium metabolism disorders.*(Wikipedia*, 2016)

### 1.10 Factors affecting calcium metabolism:

#### 1.10.1 Factors increasing absorptionof calcium

1. Vitamin D - induces the synthesis of calbindin (carrier protein for Ca) in the intestinal epithelial cells, thus increasing Ca absorption.

2. Parathyroid hormone - it increases Ca transport across the membrane of intestinal cells.

3 Acidity - Ca is more soluble and absorbed in acidic medium.

4. Lactose - it favors absorption in infants. Lactose is acted upon by intestinal microbial flora to form acid which causes lowering of pH which makes calcium more soluble.

5. Need for calcium - efficiency of calcium absorption increases according to body demands.During pregnancy, lactation and adolescence calcium absorption efficiency increases by 50%.

6. Amino acids - Lysine and arginine increases Calcium absorption.

### 1.10.2 Factors decreasing absorptionof calcium

1. Oxalic acid - It is present in vegetables. It combines with Ca to form insoluble complex calcium oxalate which cannot be absorbed.

2. Phytic acid - It is a hexaphosphate of inositol which is present in cereals. Fermentation and cooking reduces the phytate content. It is primarily found in the outer coat of cereals.

3. Malabsorption - eg: steatorrhoea. The fatty acids are not absorbed. This forms insoluble calcium salts of fatty acids.

4. Phosphate - When present in high amount it causes precipitation of calcium in the form of calcium phosphate.

Ideal ratio of Ca: P is 1:2 to 2:1.

5. Laxatives- they decrease the transit time for passage of food through intestinal tract. Thus reducing time for absorption.

6. Caffeine, drugs like anticoagulants, cortisone and thyroxine reduce calcium absorption. (*Biochemistryymt.blogspot*, 2012)

## 1.11 Effect of calcium on cell proliferation and extracellular matrix synthesis in arterial smooth muscle cells and dermal fibroblasts.

The effect of calcium on cell proliferation and connective tissue formation was studied in cultured vascular smooth muscle cells and dermal fibroblasts. Calcium deficiency caused a modest decrease in proliferation of smooth muscle cells but this effect was small compared to that previously observed with fibroblasts. Synthesis of connective tissue components was affected differently in the two cell types. Biosynthesis of proteoglycans was assessed by metabolic labeling of their glycosaminoglycan side

chains. Different levels of extracellular calcium did not affect proteoglycan production by fibroblasts, but it was significantly reduced in smooth muscle cells incubated in calcium-deficient medium. Both smooth muscle cells and fibroblasts were able to produce appreciable amounts of collagen in the complete absence of calcium and in both cell types collagen synthesis was increased when calcium was present. Fibroblasts, however, showed a much smaller response to calcium than did smooth muscle cells. In fibroblasts the maximum rate of collagen synthesis was achieved in a narrow range of calcium concentration which was slightly below that found commonly in the tissue culture medium. By contrast, in smooth muscle cells the rate of collagen synthesis increased greatly when calcium was present and this elevated rate persisted even when the cells were exposed to high levels of extracellular calcium. We conclude that these findings may be of significance to the development of atherosclerotic lesions.

### 1.11.1 Effect of calcium cell

| Cell type | Effect |
|---|---|
| Secretory cell | Increase secretion |
| Juxtaglomerular cell | Decrease secretion |
| Cell type | Effect |
| Parathyroid cell | Decrease |
| Neuron | Transmission |
| Mytocytes | Contraction |

*(Ncbi.nlm.nih.gov,2016)*

### 1.12 Calcium channel blockers

This post is an overview on calcium channel blockers, in this first part we will discuss their classification, mechanism of action as well as clinical indications.

### 1.12.1 Classification of calcium channel blockers

Calcium channel blockers comprise three chemical groups, all of them bind the L-type Calcium channel, but each class binds to different binding sites of the same channel:

- **Phenilalkylamines**: verapamil is the only drug in this group, it binds to the V binding site.
- **Benzothiazepines:** diltiazem binds to the D binding site in the L-type Calcium channel. It shows cardiovascular effects similar to those of verapamil.
- **Dihydropyridines**: the prototype agent in this group is nifedipine, a first generation dihydropyridine that binds to the N binding site. Second generation agents include isradipine, nicardipine, and felodipine. Amlodipine is considered a third generation dihydropyridine.

### 1.13 Mechanism of action and pharmacological effects of calcium

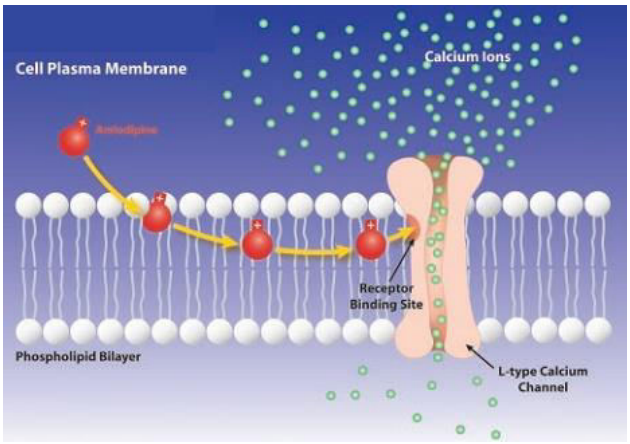



**Figure 1.1: Mechanism of action of calcium**

Calcium channel antagonists block the inward movement of calcium by binding to the L-type calcium channels in the heart and in smooth muscle of the peripheral vasculature. Calcium channel blockers dilate coronary arteries and peripheral arterioles, but not veins. They also decrease cardiac contractility (negative inotropic effect) ,automaticity at the SA node and conduction at the AV node. Dilation of the coronary arteries increases myocardial oxigen supply.

**Table:1.2- Differences in terms of tissue selectivity between dihydropiridines (nifedipine and others), diltiazem and verapamil:**

| | Peripheral and coronary vasodilation | Depression of cardiac contractility | Depression of SA node | Depression of AV node |
|---|---|---|---|---|
| Nifedipine | +++++ | + | + | 0 |
| Diltiazem | +++ | ++ | +++++ | ++++ |
| Verapamil | ++++ | ++++ | +++++ | +++++ |

Dihydropiridines have minimal effect on cardiac conduction or heart rate, while they have potent actions as arteriolar vasodilators. This class of drugs can cause reflex tachycardia when peripheral vasodilation is marked.

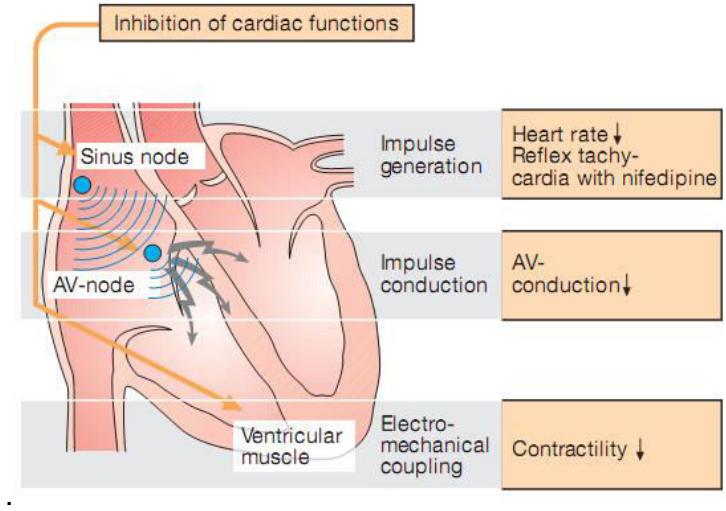



**Figure 1.2: Mechanism of dihydropyridine**

On the other hand, verapamil and diltiazem slow AV conduction and decrease SA node automaticity, they also decrease heart rate. Diltiazem is used in the treatment of variant angina because of its coronary antispasmodic properties.

### 1.14 Indications of calcium

#### 1.14.1 Hypertension

CCB's effectiveness in the treatment of hypertension is related to a decrease in peripheral resistance accompanied by increases in cardiac index.CCB are also useful in the treatment of hypertensive patients with comorbidities such as: asthma, diabetes, angina, ond or peripheral vascular disease.

#### 1.14.2 Angina pectoris

Calcium channel blockers act as coronary vasodilators, producing variable and dose-dependent reductions in myocardial oxygen demand, contractility, and arterial pressure. These combined pharmacologic effects are advantageous and make these agents as effective as beta blockers in the treatment of angina pectoris. They are indicated when beta blockers are contraindicated, poorly tolerated, or ineffective.In the presence of heart failure, the use of calcium channel blockers can cause further worsening of heart failure as a result of their negative inotropic effect.

- Supraventricular tachyarrhythmias
- Verapamil and diltiazem indications
- Verapamil and diltiazem indications

Verapamil and diltiazem are class IV antiarrhythmics, according to Vaughan and Williams' classification of antiarrhythmic drugs. This is based on their depressant action at the SA and AV nodes. Their ability to inhibit the AV node is employed in the management of supraventricular tachyarrhythmias, such as: atrial fibrillation, atrial flutter and paroxysmal supraventricular tachycardia.(*Pharmacologycorner*, 2016)

### 1.15 Possible Signs of Calcium Deficiency

Typically, there are no obvious signs of a calcium deficiency for most people until osteoporosis is discovered, either through bone scans or though a broken bone. Most of the calcium in the human body is stored in the bones and the teeth. While many people think of bones and teeth as being permanent, unchanging structures, they are actually being constantly broken down and rebuilt. It is absolutely essential to keep a certain

steady level of calcium in the blood. If blood calcium levels are too low, the body will break down bone and teeth to increase the blood calcium levels. If the blood levels are high, then the body uses the extra calcium to rebuild bone and teeth. Most of the symptoms that might occur due to a calcium deficiency would be seen only if calcium levels are low in the blood. Because the body is very good at keeping the bloodcalcium levels steady (often at the expense of bone strength), most people will never experience any symptoms of a deficiency until their bone.

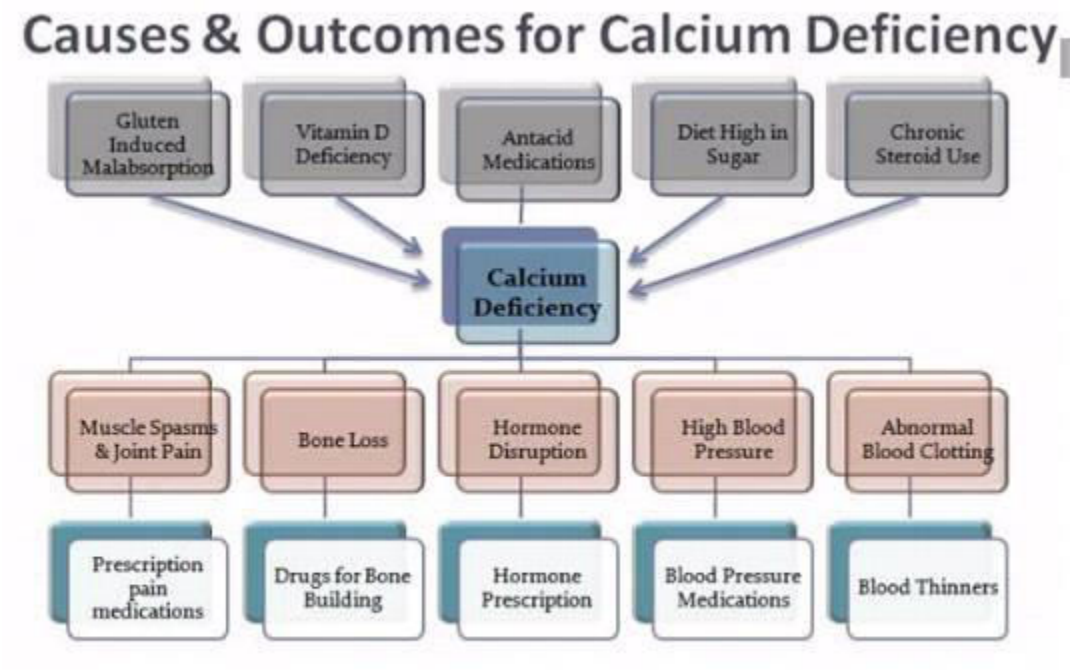



**Figure 1.3:** Calcium deficiency and its outcome (Dr. peter Osborne, 2005)

### 1.16 Disease related with calcium

#### 1.16.1 Osteoporesis

Osteoporosis is a bone disease that occurs when the body loses too much bone, makes too little bone, or both. As a result, bones become weak and may break from a fall or, in serious cases, from sneezing or minor bumps.

Osteoporosis means “porous bone.” Viewed under a microscope, healthy bone looks like a honeycomb. When osteoporosis occurs, the holes and spaces in the honeycomb are much larger than in healthy bone. Osteoporotic bones have lost density or mass and contain abnormal tissue structure. As bones become less dense, they weaken and are more likely to break. If you’re 50 or older and have broken a bone, ask your doctor or healthcare provider about a bone density test.

54 million Americans have osteoporosis and low bone mass, placing them at increased risk for osteoporosis. Studies suggest that approximately one in two women and up to one in four men age 50 and older will break a bone due to osteoporosis.

Breaking a bone is a serious complication of osteoporosis, especially with older patients. Osteoporotic bone breaks are most likely to occur in the hip, spine or wrist, but other bones can break too. In addition to causing permanent pain, osteoporosis causes some patients to lose height. When osteoporosis affects vertebrae, or the bones of the spine, it often leads to a stooped or hunched posture.

Osteoporosis may limit mobility, which often leads to feelings of isolation or depression. Additionally, twenty percent of seniors who break a hip die within one year from either complications related to the broken bone itself or the surgery to repair it. Many patients require long-term nursing home care.

Osteoporosis is responsible for two million broken bones and $19 billion in related costs every year. By 2025, experts predict that osteoporosis will be responsible for approximately three million fractures and $25.3 billion in costs annually.

Osteoporosis is often called a silent disease because one can’t feel bones weakening. Breaking a bone is often the first sign of osteoporosis or a patient may notice that he or she is getting shorter or their upper back is curving forward. If you are experiencing height loss or your spine is curving, be sure to consult your doctor or healthcare professional immediately.(*Nof.org*, 2016)

### 1.16.2 Symptoms of Osteoporesis

- **Fracture:** A fracture is one of the most common signs of fragile bones caused by osteoporosis. Fractures can occur with a fall or even a minor movement such as stepping off a curb. Osteoporosis fractures can even be triggered by a strong sneeze or cough.
- **Back or Neck Pain:** Osteoporosis can cause compression fractures of the spine. These can be very painful because the collapsed vertebrae may pinch the nerves that radiate out from the spinal cord. The pain symptoms can range from minor tenderness to debilitating pain.
- **Loss of Height:**The compression fractures in the spine can also cause a loss of height. This is one of the most noticeable symptoms of osteoporosis.
- **Stooped Posture:** The compression of the vertebrae may also cause a slight curving of the upper back. A stooped back is known as kyphosis, or more commonly as dowager's hump. Kyphosis can cause back and neck pain and even affect breathing due to extra pressure on the airway.(*Healthline*, 2016)

### 1.17Treatment of Osteoporesis

Understanding osteoporosis treatment is vital for everyone, particularly if you have risk factors for the disorder. Osteoporosis treatment includes a multifaceted regimen of diet, lifestyle habits, and osteoporosis medications in order to prevent further bone loss and fractures.

- **Osteoporosis Medications**

Osteoporosis treatments come in several forms. Many should be started during childhood; others include prescription drugs to treat osteoporosis.

- **Osteoporosis Exercise**

Weight-bearing exercise is often an option for osteoporosis patients, and it might even help your bones, as this article explains. Check with your doctor before starting a new fitness program.

- **Strontium Treatment for Osteoporosis**

If you are concerned about the bone-thinning disease osteoporosis, one treatment you may have heard of and considered is strontium.

- **Selective Estrogen Receptor Modulators**

Raloxifene (Evista) belongs to a class of drugs called selective estrogen receptor modulators .It is FDA-approved for the prevention and treatment of osteoporosis in postmenopausal women.

- **Forteo for Osteoporosis**

Teriparatide (Forteo) is self-injected into the skin. Because long-term safety is not yet established, it is only FDA-approved for 24 months of use.

(*Healthline*, 2016)

### 1.18 Diagnosis of Osteoporesis

#### 1.18.1Before any symptoms develop in human body

The ideal situation is that 'thinning' of the bones (osteoporosis) should be prevented in the first place. If this is not possible, the next best thing is for diagnosis and treatment of osteoporosis as necessary before any symptoms or fracture occur.

At present, there is no national screening programme in the UK for osteoporosis. However, if you have a risk factor, your GP or other health professional may ask you questions to see how many other risk factors for osteoporosis (listed above) apply to you. A risk calculator is available to determine your risk of developing osteoporosis, depending on the number of risk factors that you have. There are two commonly used risk calculators. One is called FRAX®, and the other is called QFracture.

If you are found to be at increased risk, or your risk is uncertain, you may be referred for a DEXA scan. DEXA stands for dual-energy X-ray absorptiometry. It is a scan that uses special X-ray machines to check your bone density. A DEXA scan can confirm osteoporosis.

### 1.18.2 After symptoms develop in human body

Osteoporosis is often first diagnosed when you break a bone after a minor bump or fall. Even after the first fracture has occurred, treatment can help to reduce your risk of further fractures. If you are thought to have sustained a fragility fracture, you will usually be referred for a DEXA scan to look for signs of osteoporosis. However, sometimes women of 75 or older who have a fracture are assumed to have had a fragility fracture. In this group of women, treatment for osteoporosis may be started without having a DEXA scan first. This is because osteoporosis is so common in this age group.

### 1.18.3 Other tests for treatment of osteoporesis

A newer test to look for osteoporosis is called digital X-ray radiogrammetry (DXR). It is easier to perform than a DEXA scan because it requires less technical equipment. It may sometimes be used as a screening test for osteoporosis - for example, in someone who has broken their wrist after a fall. However, it is not as sensitive as a DEXA scan at picking up all cases of osteoporosis. So, a DEXA scan remains the gold standard test.

Ultrasound scans are also sometimes used as a screening test. They usually assess the bone at your heel. Again, they are not as sensitive as DEXA and not used very often.(*MedicineNet*, 2016)

## 1.19Prevention of osteoporosis

Genetic factors play a significant role in determining whether an individual is at heightened risk of osteoporosis. However, lifestyle factors such as diet and physical activity also influence bone development in youth and the rate of bone loss later in life.

After your mid-20s, bone thinning is a natural process and cannot be completely stopped. The thicker your bones, the less likely they are to become thin enough to break. Young women in particular need to be aware of their osteoporosis risk and take steps to slow its progress and prevent fractures.

It’s never too early to invest in bone health. The prevention of osteoporosis begins with optimal bone growth and development in youth.

Bones are living tissue, and the skeleton grows continually from birth to the end of the teenage years, reaching a maximum strength and size (peak bone mass) in early adulthood, around the mid-20s.

- **Children**

1.Ensure a nutritious diet with adequate calcium intake

2.Avoid protein malnutrition and under-nutrition

3.Maintain an adequate supply of vitamin D

4.Participate in regular physical activity

5.Avoid the effects of second-hand smoking

- **Adults**

1.Ensure a nutritious diet and adequate calcium intake

2.Avoid under-nutrition, particularly the effects of severe weight-loss diets and eating disorders

3.Maintain an adequate supply of vitamin D

4.Participate in regular weight-bearing activity

5.Avoid smoking and second-hand smoking

6.Avoid heavy drinking

*(Iofbonehealth.org*, 2016)

### 1.20 Hypercalcemia

Calcium plays an important role in the development and maintenance of bones in the body. It is also needed in tooth formation and is important in other body functions. Normally, the body maintains a balance between the amount of calcium in food sources and the calcium already available in the body's tissues. The balance can be upset if excess amounts of calcium are eaten or if the body is unable to process the mineral because of disease.

Calcium is one of the most important and most abundant minerals in the human body. Dairy products are the major source of calcium. Eggs, green leafy vegetables, broccoli, legumes, nuts, and whole grains provide smaller amounts. Only about 10-30% of the calcium in food is absorbed into the body. Most calcium is found in combination with other dietary components and must be broken down by the digestive system before it can be used. Calcium is absorbed into the body in the small intestine. Its absorption is influenced by such factors as the amount of vitamin D hormone available to aid the process and the levels of calcium already present in the body. As much as 99% of the body's calcium is stored in bone tissue. A healthy person experiences a constant turnover of calcium as bone tissue is built and reshaped. The remaining 1% of the body's calcium circulates in the blood and other body fluids. Circulating calcium plays an important role in the control of many body functions, such as blood clotting, transmission of nerve impulses, muscle contraction, and other metabolic activities. In the bloodstream, calcium maintains a constant balance with another mineral, phosphate.

Two main control agents are vital in maintaining calcium levels, vitamin D hormone and parathyroid hormone. A hormone is a chemical substance that is formed in one organ or part of the body and carried in the blood to another organ. It can alter the function, and sometimes the structure, of one or more organs.

Parathyroid hormone. The four parathyroid glands are endocrine glands located next to the thyroid gland in the neck. A gland is a cell or group of cells that produces a material substance (secretion). When the level of calcium circulating in the blood drops, the parathyroid gland releases its hormone. Parathyroid hormone then acts in three ways to

restore the normal blood calcium level. It stimulates the absorption of more calcium in the intestine; it takes more calcium from the bone tissue, and it causes the kidneys to excrete more phosphate.

Vitamin D hormone. This hormone works with parathyroid hormone to control calcium absorption and affects the deposit of calcium and phosphate in the bone tissue.

The kidneys also help to control calcium levels. Healthy kidneys can increase calcium excretion almost fivefold to maintain normal concentrations in the body. Hypercalcemia can occur when the concentration of calcium overwhelms the ability of the kidneys to maintain balance.(*TheFreeDictionary*, 2016)

### 1.20.1 Signs and symptoms of Hypercalcemia

- The neuromuscular symptoms of hypercalcemia are caused by a negative bathmotropic effect due to the increased interaction of calcium with sodium channels. Since calcium blocks sodium channels and inhibits depolarization of nerve and muscle fibers, increased calcium raises the threshold for depolarization.
- Stones (renal or biliary)
- Bones (bone pain)
- Groans (abdominal pain, nausea and vomiting)
- Thrones (polyuria) resulting in dehydration
- Psychiatric overtones (Depression 30–40%, anxiety, cognitive dysfunction, insomnia, coma)
- Other symptoms can include fatigue, anorexia, and pancreatitis. Limbus sign seen in eye due to hypercalcemia.

Hypercalcaemia has also been known to cause an ECG finding mimicking hypothermia, known as an Osborn wave.Hypercalcaemia can increase gastrin production, leading to increased acidity so peptic ulcers may also occur.

Symptoms are more common at high calcium blood values (12.0 mg/dL or 3 mmol/l).The high levels of calcium ions at these levels. Severecoma and cardiac arrest can result hypercalcaemia (above 15–16 mg/dL or 3.75–4 mmol/l) is considered a

medical decrease the neuron membrane permeability to sodium ions, thus decreasing the excitability, which leads to hypotonicity of smooth and striated muscle. This explains the fatigue, muscle weakness, low tone and sluggish reflexes in muscle groups. The sluggish nerves also explain drowsiness, confusion, hallucinations, stupor and / or coma. In the gut this causes constipation. Hypocalcaemia causes the opposite by the same mechanism.(*Wikipedia*, 2016)

### 1.20.2 Causes of Hypercalcemia

Primary hyperparathyroidism and malignancy account for about 90% of cases of hypercalcaemia..

- **Parathyroid function**
  - ✓ primary hyperparathyroidism
  - ✓ solitary parathyroid adenoma
  - ✓ primary parathyroid hyperplasia
  - ✓ parathyroid carcinoma
  - ✓ multiple endocrine neoplasia
  - ✓ familial isolated hyperparathyroidism
  - ✓ lithium use
  - ✓ familial hypocalciurichypercalcaemia/familial benign hypercalcaemia

- **Cancer:** Micrograph of ovarian small cell carcinoma of the hypercalcemic type. H&E stain solid tumour with metastasisolid tumour with humoral mediation of hypercalcaemia (e.g. lung cancer, most commonly non-small cell lung cancer or kidney cancer, phaeochromocytoma)haematologic malignancy (multiple myeloma, lymphoma, leukaemia)ovarian small cell carcinoma of the hypercalcemic type.

### 1.20.3 Treatments of Hypercalcemia

The goal of therapy is to treat the hypercalcaemia first and subsequently effort is directed to treat the underlying cause.

- **Initial therapy:** fluids and diuretics

Hydration, increasing salt intake, and forced diuresis. Hydration is needed because many patients are dehydrated due to vomiting or renal defects in concentrating urine increased salt intake also can increase body fluid volume as well as increasing urine sodium excretion, which further increases urinary potassium excretion after rehydration, a loop diuretic such as furosemide can be given to permit continued large volume intravenous salt and water replacement while minimizing the risk of blood volume overload and pulmonary oedema. In addition, loop diuretics tend to depress renal calcium reabsorption thereby helping to lower blood calcium levels can usually decrease serum calcium by 1–3 mg/dL within 24 h caution must be taken to prevent potassium or magnesium depletionAdditional therapy: bisphosphonates and calcitonin bisphosphonates are pyrophosphate analogues with high affinity for bone, especially areas of high bone-turnover they are taken up by osteoclasts and inhibit osteoclastic bone resorption current available drugs include (in order of potency): (1st gen) etidronate, (2nd gen) tiludronate, IV pamidronate, alendronate (3rd gen) zoledronate and risedronate all patients with cancer-associated hypercalcaemia should receive treatment with bisphosphonates since the 'first line' therapy (above) cannot be continued indefinitely nor is it without risk. Further, even if the 'first line' therapy has been effective, it is a virtual certainty that the hypercalcaemia will recur in the patient with hypercalcaemia of malignancy. Use of bisphosphonates in such circumstances, then, becomes both therapeutic and preventative patients in renal failure and hypercalcaemia should have a risk-benefit analysis before being given bisphosphonates, since they are relatively contraindicated in renal failure. Calcitonin blocks bone resorption and also increases urinary calcium excretion by inhibiting renal calcium reabsorption Usually used in life-threatening hypercalcaemia along with rehydration, diuresis, and bisphosphonates Helps prevent recurrence of hypercalcaemia .Dose is 4 Units per kg via subcutaneous or intramuscular route every 12 hours, usually not continued indefinitely

- **Other therapies of Hypercalcemia**

1. plicamycin inhibits bone resorption (rarely used)
2. gallium nitrate inhibits bone resorption and changes structure of bone crystals (rarely used)
3. glucocorticoids increase urinary calcium excretion and decrease intestinal calcium absorption
4. no effect on calcium level in normal or primary hyperparathyroidism

Effective in hypercalcaemia due to osteolytic malignancies (multiple myeloma, leukaemia, Hodgkin's lymphoma, carcinoma of the breast) due to antitumour properties also effective in hypervitaminosis D and sarcoidosis dialysis usually used in severe hypercalcaemia complicated by renal failure. Supplemental phosphate should be monitored and added if necessary phosphate therapy can correct the hypophosphataemia in the face of hypercalcaemia and lower serum calcium. *Wikipedia*, 2016

### 1.21 Hypocalcemia

Blood calcium is tightly regulated within a narrow range for proper cellular processes. Calcium in the blood exists in three primary states: bound to proteins (mainly albumin), bound to anions such as phosphate and citrate, and as free (unbound) ionized calcium. Only the ionized calcium is physiologically active. Normal blood calcium level is between 8.5 to 10.5 mg/dL (2.12 to 2.62 mmol/L) and that of ionized calcium is 4.65 to 5.25 mg/dL (1.16 to 1.31 mmol/L). Common causes of hypocalcemia include hypoparathyroidism, vitamin D deficiency, and chronic kidney disease. Symptoms of hypocalcemia include neuromuscular irritability (including tetany as manifested by Chvostek's sign or Trousseau's sign, bronchospasm), electrocardiographic changes, and seizures. Treatment is dependent upon the cause, but most commonly includes supplementation of calcium and some form of vitamin D or its analogues.

Hypocalcaemia or hypocalcemia is the presence of low serum calcium levels in the blood. Physiologically

### 1.21.1 Signs and symptoms of hypocalcemia

The neuromuscular symptoms of hypocalcemia are caused by a positive bathmotropic effect due to the decreased interaction of calcium with sodium channels. Since calcium blocks sodium channels and inhibits depolarization of nerve and muscle fibers, diminished calcium lowers the threshold for depolarization.

1. The symptoms can be recalled by the mnemonic "CATS go numb"- Convulsions, Arrhythmias, Tetany and numbness/parasthesias in hands, feet, around mouth and lips.

2. Petechiae which appear as on-off spots, then later become confluent, and appear as purpura (larger bruised areas, usually in dependent regions of the body).

3.Oral, perioral and acralparesthesias, tingling or 'pins and needles' sensation in and around the mouth and lips, and in the extremities of the hands and feet. This is often the earliest symptom of hypocalcaemia.

4.Carpopedal and generalized tetany (unrelieved and strong contractions of the hands, and in the large muscles of the rest of the body) are seen.

5.Latent tetany Trousseau sign of latent tetany (eliciting carpal spasm by inflating the blood pressure cuff and maintaining the cuff pressure above systolic)

6.Life-threatening complications

7.Laryngospasm

8.Cardiac arrhythmias

9.Effects on cardiac output

10.Positive chronotropic effect, or an increase in heart rate

11.Negative inotropic effect, or a decrease in contractility

### 1.21.2 Causes of Hypocalcemia

This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. (March 2014)

Hypoparathyroidism is a common cause of hypocalcemia. Calcium is tightly regulated by the parathyroid hormone .In response to low calcium levels, parathyroid hormone induces the kidneys to reabsorb calcium, the kidneys to increase production of calcitriol (the active form of vitamin D) thereby increasing intestinal absorption of calcium, and the bones to release calcium. These actions lead to a re-balance in the blood calcium levels. However, in the setting of absent, decreased, or ineffective parathyroid hormone, the body loses this regulatory function, and hypocalcemia ensues. Hypoparathyroidism is commonly due to surgical destruction of the parathyroid glands via parathyroidectomy or neck dissection for head and neck cancers. Hypoparathyroidism may also be due to autoimmune destruction of the glands.

- **Eating disorders**
  - ✓ Prolonged vomiting (e.g. with a viral illness)
  - ✓ Exposure to mercury, including infantile acrodynia
  - ✓ Excessive dietary magnesium, as with supplementation.
  - ✓ Excessive dietary zinc, as with supplementation (causes rapid hypocalcemia).
  - ✓ Prolonged use of medications/laxatives containing magnesium
  - ✓ Chelation Therapy for metal exposure, particularly EDTA
  - ✓ Osteoporosis treatment or preventive agents, such as Bisphosphonates and Denosumab.
  - ✓ Agents for the treatment of hypercalcemia, such as Calcitonin.
  - ✓ Chronic kidney failure
  - ✓ Absent active vitamin D
  - ✓ Decreased dietary intake
  - ✓ Decreased sun exposure
  - ✓ Defective Vitamin D metabolism
  - ✓ Vitamin-D dependent rickets, type I

- ✓ Vitamin-D dependent rickets, type II
- ✓ Pseudohypoparathyroidism
- ✓ Severe acute hyperphosphataemia
- ✓ Tumour lysis syndrome
- ✓ Acute kidney failure
- ✓ Rhabdomyolysis (initial stage)
- ✓ Exposure to hydrofluoric acid

### 1.21.3 Diagnosis of Hypocalcemia

Because a significant portion of calcium is bound to albumin, any alteration in the level of albumin will affect the level of calcium is measured. A corrected calcium level based on the albumin level is: Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8 * (4.0 - serum albumin [g/dL]). Another way to determine the calcium level is to measure directly the ionized calcium level.

### 1.21.4 Management of Hypocalcemia

Intravenous calcium gluconate 10% can be administered, or if the hypocalcaemia is severe, calcium chloride is given instead. This is only appropriate if the hypocalcemia is acute and has occurred over a relatively short time frame. But if the hypocalcemia has been severe and chronic, then this regimen can be fatal, because there is a degree of acclimatization that occurs. The neuromuscular excitability, cardiac electrical instability, and associated symptoms are then not cured or relieved by prompt administration of corrective doses of calcium, but rather exacerbated. Such rapid administration of calcium would result in effective over correction – symptoms of hypercalcemia would follow.

However, in either circumstance, maintenance doses of both calcium and vitamin-D are often necessary to prevent further decline.

Hypocalcaemia or hypocalcemia is the presence of low serum calcium levels in the blood. Physiologically, blood calcium is tightly regulated within a narrow range for proper cellular processes. Calcium in the blood exists in three primary states: bound to proteins (mainly albumin), bound to anions such as phosphate and citrate, and as free (unbound) ionized calcium. Only the ionized calcium is physiologically active. Normal blood calcium level is between 8.5 to 10.5 mg/dL (2.12 to 2.62 mmol/L) and that of ionized calcium is 4.65 to 5.25 mg/dL (1.16 to 1.31 mmol/L). Common causes of hypocalcemia include hypoparathyroidism, vitamin D deficiency, and chronic kidney disease. Symptoms of hypocalcemia include neuromuscular irritability (including tetany as manifested by Chvostek's sign or Trousseau's sign, bronchospasm), electrocardiographic changes, and seizures. Treatment is dependent upon the cause, but most commonly includes supplementation of calcium and some form of vitamin D or its analogues..(*Proceedings of the National Academy of Sciences*, 1999)

### 1.22 Awareness of Vitamin D

Vitamin D deficiency exists when the concentration of 25-hydroxy-vitamin D in the blood serum occurs at 12 ng/ml (nanograms/milliliter), or less. The normal concentration of 25-hydroxy-vitamin D in the blood serum is 25-50 ng/ml. When vitamin D deficiency continues for many months in growing children, the disease commonly referred to as rickets will occur. A prolonged deficiency of the vitamin in adults results in osteomalacia. Both diseases involve defects in bones.

### 1.23 Description of Vitamin D

Vitamin D is a fat-soluble vitamin, meaning it is able to be dissolved in fat. While some vitamin D is supplied by the diet, most of it is made in the body. To make vitamin D, cholesterol, a sterol that is widely distributed in animal tissues and occurs in the yolk of eggs, as well as in various oils and fats, is necessary. Once cholesterol is available in the body, a slight alteration in the cholesterol molecule occurs, with one change taking place in the skin. This alteration requires the energy of sunlight (or ultraviolet light). Vitamin D deficiency, as well as rickets and osteomalacia, tends to occur in persons who do not get enough sunlight and who fail to eat foods that are rich in vitamin D.Once consumed, or made in the body, vitamin D is further altered to produce a hormone

called 1,25-dihydroxy-vitamin D. The conversion of vitamin D to 1,25-diOH-D does not occur in the skin, but in the liver and kidney. First, vitamin D is converted to 25-OH-D in the liver; it then enters the bloodstream, where it is taken-up by the kidneys. At this point, it is converted to 1.25-diOH-D. Therefore, the manufacture of 1,25-diOH-D requires the participation of various organs of the body—the liver, kidney, and skin.

The purpose of 1, 25-diOH-D in the body is to keep the concentration of calcium at a constant level in the bloodstream. The maintenance of calcium at a constant level is absolutely required for human life to exist, since dissolved calcium is required for nerves and muscles to work. One of the ways in which 1, 25-diOH-D accomplishes this mission is by stimulating the absorption of dietary calcium by the intestines.

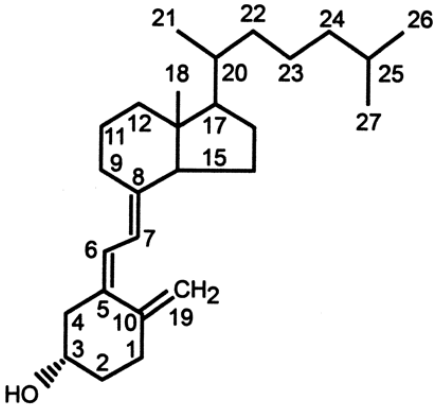
The sequence of events that can lead to vitamin D deficiency, then to bone disease, is as follows: a lack of vitamin D in the body creates an inability to manufacture 1,25-diOH-D, which results in decreased absorption of dietary calcium and increased loss of calcium in the feces. When this happens, the bones are affected. Vitamin D deficiency results in a lack of bone mineralization (calcification) in growing persons, or in an increased demineralization (decalcification) of bone in adults in D.(*TheFreeDictionary*, 2016)

**1.24 Mechanism of vitamin D in human body**

Vitamin D is normally produced in skin through a robust photolytic process acting on a derivative of cholesterol (i.e. 7-dehydrocholesterol) to produce previtamin D, which is then slowly isomerized to vitamin D3. Vitamin D3 is the natural form of vitamin D produced in skin, and vitamin D2 is derived from irradiation of ergosterol, which occurs to some degree in plankton under natural conditions and is used to produce vitamin D2 from the mold ergot (which contains as much as 2% ergosterol). We must move away from the concept that vitamin D is a vitamin.

Another important fact is that vitamin D is required throughout life. It not only is needed for the formation of bone but also likely plays an important role in several other physiologic systems. Its use may well prevent several degenerative diseases, and it may also play a role as an anticancer agent.

The structure of vitamin D3 and its numbering system are indicated in Figure 1⇓. We now know that vitamin D3 itself is biologically inert, as clearly indicated by genetic defects that result in the disease rickets despite normal intakes of vitamin D. By 1967, the concept that vitamin D is converted to an active form had appeared. By 1969, the circulating form of vitamin D had been isolated, chemically identified, and synthesized. This compound, 25-hydroxyvitamin D3, is now currently monitored in serum to indicate the vitamin D status of patients, as discussed below. However, VitaminD3 itself is metabolically inactive and must be modified before function. The final active hormone derived from vitamin D was isolated and identified in 1971, and its structure was deduced as 1α,25-dihydroxyvitamin D3 and confirmed by synthesis. For 2 decades, there was consistent revisitation of the concept that more than one hormone was derived from vitamin D, and ~33 metabolites of vitamin D were identified. However, it soon became clear that all metabolites were either less active or rapidly cleared and were thus intermediates in the degradation of this important molecule. The most important of these metabolites are 24,25-dihydroxyvitamin D3 and 1α,24(R),25-trihydroxyvitamin D3 produced by the enzyme CYP24, which is induced by the vitamin D hormone itself.




Vitamin $D_3$

Much is known about the enzymes that produce 1,25(OH)2D3 and their regulation, but a great deal remains to be learned. Two enzymes are thought to function in the 25-hydroxylation step. They are not exclusively hepatic but are largely functionally active in the liver. The mitochondrial enzyme, which is not specific for vitamin D, has been cloned and a knockout mouse strain has been prepared, without any apparent effect on vitamin D metabolism, which suggests that there is an alternate 25-hydroxylase. A microsomal hydroxylase was recently cloned and could represent the missing enzyme. The 25(OH)D3 1α-hydroxylase was cloned by 3 different laboratories, and the sites of vitamin D-dependent rickets type I were identified in several studied. Very important was the generation of 1α-hydroxylase knockout mice, which exhibit a phenotype virtually identical to the human vitamin D-dependent rickets type I phenotype. Therefore, the enzymes that activate vitamin D have been identified.

Of major metabolic importance is the mode of disposal of vitamin D and its hormonal forms. The cytochrome P-450 enzyme now called CYP24 was isolated in pure form by Ohyama and Okuda and the complementary DNA and gene were cloned, which yielded a 24-hydroxylase-null mutant. No significant phenotype resulted except for a large accumulation of 1,25(OH)2D3 in the circulation, which produced secondary effects on cartilaginous growth. CYP24 is an extremely active enzyme, but the gene remains silent in vitamin D deficiency; it is induced by the hormonal form of vitamin D itself. Therefore, pulses of the vitamin D hormone program its own death through induction of the 24-hydroxylase. The 24-hydroxylase is able to metabolize vitamin D to its excretion product calcitroic acid. 25(OH)D3 can also be degraded through this pathway. 24-Hydroxylase and its regulation are important factors in the determination of the circulating concentrations of the hormonal form of vitamin D.

### 1.25 Physiologic function of Vitamin D

The role of the vitamin D hormone in mineralizing the skeleton and preventing hypocalcemic tetany. Plasma calcium concentrations are maintained at a very constant level, and this level is supersaturating with respect to bone mineral. If the plasma becomes less than saturated with respect to calcium and phosphate, then mineralization fails, which results in rickets among children and osteomalacia among adults. The vitamin D hormone functions to increase serum calcium concentrations through 3 separate activities. First, it is the only hormone known to induce the proteins involved in active intestinal calcium absorption. Furthermore, it stimulates active intestinal absorption of phosphate. Second, blood calcium concentrations remain in the normal range even when an animal is placed on a no-calcium diet. Therefore, an animal must possess the ability to mobilize calcium in the absence of calcium coming from the environment, ie, through enterocytes. Two mechanisms play a role in increasing blood calcium concentrations, especially in the absence of intestinal calcium absorption. Vitamin D hormone stimulates osteoblasts to produce receptor activator nuclear factor-κB ligand (RANKL). RANKL then stimulates osteoclastogenesis and activates resting osteoclasts for bone resorption. Therefore, the vitamin D hormone plays an important role in allowing individuals to mobilize calcium from bone when it is absent from the diet. It is very important to note, however, that in vivo both vitamin D and parathyroid hormone are required for this mobilization event. Therefore, 2 keys are required, similar to a safety deposit box. Third, the distal renal tubule is responsible for reabsorption of the last 1% of the filtered load of calcium, and the 2 hormones interact to stimulate the reabsorption of this last 1% of the filtered load. Because 7 g of calcium are filtered every day among humans, this represents a major contribution to the calcium pool. Again, both parathyroid hormone and the vitamin D hormone are required. Calcium physiologic processes are such that a single low concentration of the vitamin D hormone stimulates enterocytes to absorb calcium and phosphate. If the plasma calcium concentration fails to respond, then the parathyroid glands continue to secrete parathyroid hormone, which increases production of the vitamin D hormone to mobilize bone calcium (acting with parathyroid hormone). Under normal circumstances, environmental calcium is used first; if environmental calcium is absent, then internal stores are use .Diagrammatic

representation of the role of the vitamin D hormone and the parathyroid hormone in increasing plasma calcium concentrations to prevent hypocalcemic tetany

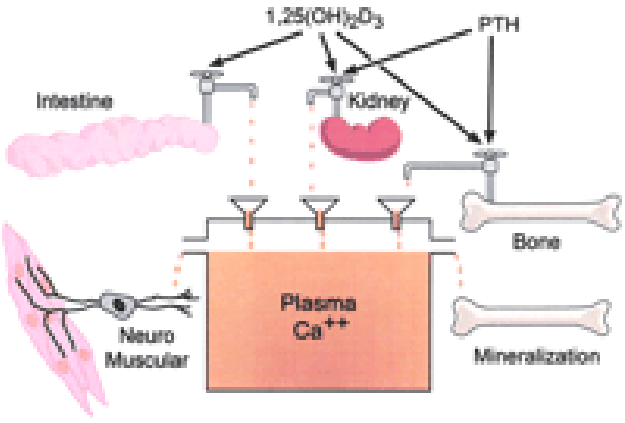



**Figure 1.4: Vitamin D Endocrine System**

A diagrammatic representation of the endocrine regulation of calcium concentrations in the plasma and the vitamin D endocrine system is presented. Calcium-sensing proteins that sense plasma calcium concentrations are found in the parathyroid gland. When calcium concentrations decrease below normal, even slightly, then these transmembrane proteins, coupled to a G protein system, stimulate the secretion of parathyroid hormone. Parathyroid hormone then proceeds to the osteoblasts and to the proximal convoluted tubule cells within seconds. Most importantly, in the convoluted tubule cells that serve as the endocrine gland for the vitamin D hormone, 1α-hydroxylase concentrations are markedly elevated. This signals the vitamin D hormone, which by itself stimulates intestinal absorption of calcium or together with parathyroid hormone, at higher concentrations, stimulates mobilization of bone calcium and renal reabsorption of calcium. The increase in serum calcium concentrations exceeds the set point of the calcium-sensing system, shutting down the parathyroid gland-induced cascade of events. If the plasma calcium concentrations overshoot, then the C-cells of the thyroid gland secrete the 32-amino acid peptide calcitonin, which blocks bone calcium mobilization. Calcitonin also stimulates the renal 1α-hydroxylase to provide the vitamin D hormone for noncalcemic needs under normocalcemic conditions.The molecular mechanisms have not been entirely determined, except for the vitamin D hormone induction of 24-hydroxylase (CYP24).

An important aspect of the vitamin D endocrine system is that dietary calcium is favored to support serum calcium concentrations under normal conditions but, when this fails, the system mediates calcium mobilization from bone and reabsorption in the kidney to satisfy the needs of the organism. This results in loss of calcium from the skeleton and can ultimately lead to osteoporosis. Another important aspect is that, except for stimulating mineralization of the skeleton, the vitamin D hormone has not been found to be anabolic on bone.(*The American Journal of Clinical Nutrition*, 2004)

**1.26 Physiology of Vitamin D**

Vitamin D can be produced in the skin as vitamin D3 on exposure to ultraviolet-B from the sun or obtained from the diet as vitamin D2 or vitamin D3. After vitamin D enters the body, it circulates bound to vitamin D-binding protein and is rapidly converted to its major circulating form, 25-hydroxyvitamin D by the liver. Under the influence ofparathyroid hormone , 25(OH)D is converted by the 1-alpha-hydroxylase (1α-OHase) in the kidney to form the hormonal form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D). Other tissues in the body have the 1α-OHase and can convert 25(OH)D to 1,25(OH)2D.5 However, only the renal 1α-OHase significantly contributes to circulating 1,25(OH)2D levels. It is speculated that the presence of the extrarenal 1α-OHases allow 25(OH)D to be converted to 1,25(OH)2D to work as a paracrine or autocrine hormone.

Circulating 1,25(OH)2D enters the target cell, either in its free form or facilitated by megalin, and binds to the cytoplasm, which then translocates to the nucleus and heterodimerizes with the retinoic × receptor.6 The 1,25(OH)2D-VDR-retinoic × receptor complex then binds to vitamin D response elements on DNA to increase transcription of vitamin D-regulated genes. Classic functions regulated by vitamin D include genes important for mineralization of bone and calcium transport in the intestine.7 Nonclassic or novel functions of vitamin D under investigation include genes important for innate immunity, cancer proliferation, muscle (both skeletal and smooth) function, and endothelial cell proliferation.5

Vitamin D status is best determined by a serum 25(OH)D as opposed to 1,25(OH)2D, for several reasons including (1) its long circulating half life (~3 weeks versus ~8 hours);

(2) the concentration of 25(OH)D is 1000× higher in circulation compared with 1,25(OH)2D (ng/mL versus pg/mL); and (3) the production of 1,25(OH)2D is mainly under the influence of parathyroid hormone, which tightly regulates calcium levels. Thus, 1,25(OH)2D levels could be elevated in individuals with severe vitamin D deficiency to maintain normal serum calcium levels. As a mediator of CVD, it is believed that 25(OH)D is the best biomarker to describe vitamin D status, although this has not been proven.(*The American Journal of the Medical Sciences*, 2009)

### 1.27 Sources of Vitamin D

Vitamin D is really two different compounds, cholecalciferol (vitamin D2), found mainly in

plants and ergocalciferol (vitamin D3), found mainly in animals. Both of these hormones

are collectively referred to as vitamin D, and they can either be obtained in two ways. One

is by exposure of the skin to the ultraviolet rays of sunlight or also from dietary intake.

Vitamin D is found naturally in fish (such as salmon and sardines) and fish oils, eggs and

cod liver oil. However most Vitamin D is obtained from foods fortified with Vitamin D,

especially milk and orange juice. Interestingly, as breast feeding has become more popular,

the incidence of Vitamin D deficiency has increased as less fortified milk is consumed.

Vitamin D deficiency may also occur in patients with malabsorption from their intestine,

such as in the autoimmune disease called Celiac Disease, which occurs frequently in

patients with thyroid problems. Multivitamins also contain Vitamin D, as does some

calcium supplements like Oscal-D and Citracal plus D.

### 1.28 Vitamin-D disorders

- hypervitaminosis D (vitamin D intoxication)
- idiopathic hypercalcaemia of infancy
- rebound hypercalcaemia after rhabdomyolysis
- High bone-turnover rates
- Hyperthyroidism
- prolonged immobilization
- thiazide use
- vitamin A intoxication
- multiple myeloma
- Kidney failuresevere secondary hyperparathyroidism
- aluminium intoxication

### 1.29 Physiologycal Roles of Vitamin D

Favor calcium absorption from the intestine  Promotes the absorption of phosphate  Assist to govern the equilibrium between bone calcium and blood calcium.  Promotes calcium mobilization from bone via reabsorption  Helps in development of normal teeth.  Maintain normal structure of bone and necessary for proper bone growth.  Controls the retention of calcium and parathyroid level.  Lowers the pH of colon, caecum, ileum and increase the urinary pH simultaneously.  Increase the citrate concentration in bone, blood and other tissue (Chatterjee, 1985**).**

### 1.30 Vitamin D containing food

a) Salmon, Mackerel and Other Fatty Fish

b) Vitamin D3 Fortified Milk or Raw milkmin

c) Butter, Cheese, Egg

d) Cod Liver Oil and Other Fish Oils

e) Beef Liver, Chicken Liver and Pork Liver f) Mushrooms

Very few foods in nature are good sources of vitamin D. This is one of the main reasons that vitamin D deficiency is so common, since it's very easy to leave these foods out of our diet.

- **Salmon, Mackerel and Other Fatty Fish**

Just 3 ounces of salmon, mackerel or other fatty fish contain over 400 IU of vitamin D. This amount alone is enough to prevent many deficiency-related issues such as rickets or depression.

- **Vitamin D3 Fortified Milk or Raw Milk**

While the pasteurization process destroys much of milk's natural vitamin D content, most pasteurized milk is fortified with vitamin D3 to compensate. Drinking a glass or two of milk each day will help, and if we have access to raw milk and can afford it, it's a great investment in our health.

- **Butter, Cheese and Eggs**

Like milk, all of these products contain vitamin D but it's difficult to eat them in high enough quantities to really compensate for a lack of sun exposure. One egg, for example, only has about 40 IU of vitamin D. keep in mind though that most people get the majority of their vitamin D intake from sun exposure.

- **Cod Liver Oil and Other Fish Oils**

Perhaps it is the best natural source of vitamin D. One tablespoon of cod liver oil contains 1,360 IU of vitamin D. If we're worried about deficiency, cod liver oil (and other fish oils to a lesser extent) is great sources.

- **Beef Liver, Chicken Liver and Pork Liver**

These and some other organ meats contain vitamin D, but to a lesser degree than cod liver oil. Liver and other organ meats offer a host of other health benefits, so it's worth incorporating them into our diet even if you're vitamin D levels are sufficient.

- **Other Fortified Foods**

Many foods are now fortified with vitamin D, Which can range from margarine to breakfast cereals. The trouble with many of these foods is that they tend to be otherwise unhealthy. If we're unable to get sufficient vitamin D intake without eating fortified processed foods, it's generally best to eat more whole foods and take a vitamin D supplement.

- **Sun Exposure as a Source of Vitamin D in skin**

Exposing our self to sunlight is the most important source of vitamin D because sunlight is far more likely to provide without vitamin D requirement than food. UV rays from the sun trigger vitamin D production in our skin. Lights from our home are not strong enough to produce vitamin D. Season, geographic latitude, time of day, cloud cover, smog, and sunscreen affect UV ray exposure and vitamin D synthesis Vitamin D is essential for the control of normal calcium and phosphate blood levels.(Guyton, 2003).

### 1.31 Symptoms of Vitamin D deficiency

#### 1.31.1 Symptoms in babies and children

Babies with severe vitamin D deficiency can get muscle spasms (cramps), seizures and breathing difficulties. These problems are related to consequent low levels of calcium.

Children with severe deficiency may have soft skull or leg bones. Their legs may look curved (bow-legged). They may also complain of bone pains, often in the legs, and muscle pains or muscle weakness. This condition is known as rickets.

Poor growth. Height is usually affected more than weight. Affected children might be reluctant to start walking.

Tooth delay. Children with vitamin D deficiency may be late teething as the development of the milk teeth has been affected.

Irritability in children can be due to vitamin D deficiency.

Children with vitamin D deficiency are more prone to infections. Breathing (respiratory) symptoms can occur In severe cases. Breathing can be affected because of weak chest muscles and a soft ribcage.

When rickets if very severe, it can cause low levels of calcium in the blood. This can lead to muscle cramps (spasms), fits (seizures) and breathing difficulties. These need urgent hospital treatment.

Rarely, an extremely low vitamin D level can cause weakness of the heart muscle (cardiomyopathy).

### 1.31.2 Symptoms in adults

Some people complain of a general tiredness, vague aches and pains and a general sense of not being well.

In more severe deficiency (known as osteomalacia), there may be more severe pain and also weakness. Muscle weakness may cause difficulty in climbing stairs or getting up from the floor or a low chair, or can lead to the person walking with a waddling pattern.

Bones can feel painful to moderate pressure (often more noticeable in the ribs or shin bones). Not uncommonly, people have a hairline fracture in the bone which is causing tenderness and pain. Bone pain often also occurs in the lower back, hips, pelvis, thighs and feet.

### 1.32 Treatment for vitamin D deficiency

- **Injection**

A single small injection of vitamin D will last for about six months. This is a very effective and convenient treatment. It is useful for people who do not like taking medicines by mouth, or who are likely to forget to take their tablets.

- **High-dose tablets or liquids**

There are different strengths available and a dose may be taken either daily, weekly or monthly. This will depend on your situation and on which particular treatment guideline your doctor is using. Always check with your doctor that you understand the instructions - with high doses of vitamin D it is important to take the medicine correctly. The advantage of the higher-dose treatment is that the deficiency improves quickly - important in growing children**.**

- **Standard-dose tablets, powders or liquids**

These are taken every day for about 12 months so that the body can catch up on the missing vitamin D. This is a rather slow method of replacing vitamin D, but is suitable if the deficiency is mild, or for prevention**.**

- **Maintenance therapy after Vitamin D deficiency has been treated**

Once vitamin D deficiency has been treated, the body's stores of vitamin D have been replenished. After this, maintenance treatment is often needed long-term, to prevent further deficiency in the future. This is because it is unlikely that any risk factor for vitamin D deficiency in the first place will have completely resolved. The dose needed for maintenance may be lower thaAll pregnant and breast-feeding women should take a daily supplement containing 10 micrograms of vitamin D.

- **Prevention of Vitamin D deficiency**

All babies and young children aged 6 months to 5 years should take a daily supplement containing vitamin D in the form of vitamin drops. However, those babies who are fed infant formula will not need vitamin drops until they are receiving less than 500ml of infant formula a day, as these products are fortified with vitamin D. Breast-fed babies may need to receive drops containing vitamin D from one month of age if their mother has not taken vitamin D supplements throughout pregnancy.

People aged 65 years and over and people who are not exposed to much sun should also take a daily supplement containing 10 micrograms of vitamin D.

In addition a doctor may advise routine vitamin D supplements for people with certain gut, kidney or liver diseases, people prescribed certain medicines, and to certain people with darker skin.

You can buy vitamin D supplements at pharmacies. They are also available on prescription to certain groups of people. Women and children from families who are eligible for the Government's Healthy Start scheme can also get free vitamin supplements which include vitamin D.

If you are unsure as to whether you should be taking a regular supplement of vitamin D, or what the appropriate dose is, then your doctor, pharmacist, health visitor or midwife can advise.  that needed to treat the deficiency**.(***BMJ* 340, 2010)

**1.33 Diseases related with Vitamin D**

Vitamin D deficiency has been shown to play a role in almost every major disease. This includes:

1. Osteoporosis and Osteopenia
2. 17 varieties of Cancer (including breast, prostate and colon)
3. Heart disease
4. High blood pressure
5. Obesity
6. Metabolic Syndrome and Diabetes
7. Autoimmune diseases
8. Multiple sclerosis
9. Rheumatothritis and Osteoarthritis
10. Bursitis
11. Gout
12. Infertility and PMS
13. Parkinson's Disease
14. Depression and Seasonal Affective Disorder
15. Fibromyalgia

*(WebMD*, 2016)

### 1.34Hydroxylation of Vitamin D

The initial step in vitamin D activation occurs in the liver, where cholecalciferol and ergocalciferol are hydroxylated in the 25-position to generate 25-OH-cholecalciferol and 25-OH-ergocalciferol, respectively. Vitamin D is the major circulating form of vitamin D3; it has a biological half-life of 19 days, and normal steady-state concentrations are 15 to 50 mg/ml. Reduced extracellular Calcium levels stimulate 1a-hydroxylation of Calcitriol, increasing the formation of biologically active 1,25(OH)2D3. In contrast, when Calcium concentrations are elevated, Calcitriol is inactivated by 24-hydroxylation. Similar reactions occur with 25-OH-ergocalciferol. Normal steady-state concentrations of Calcitriol in human beings are 15 to 50 mg/ml, although concentrations below 25 mg/ml may be associated with increased circulating parathyroid hormone and greater bone turnover.

24-Hydroxylase Calcitriol and 25-OHD are hydroxylated to 1, 24, 25(OH)2D and 24,25(OH)2D, respectively, by another renal enzyme, 24-hydroxylase, whose expression is induced by calcitriol and suppressed by factors that stimulate the 25-OHD-1a-hydroxylase. Both24-hydroxylated compounds are less active than calcitriol and presumably represent metabolites destined for excretion

Active vitamin D functions as a hormone, and its main biologic function in people is to maintain serum calcium and phosphorus concentrations within the normal range by enhancing the efficiency of the small intestine to absorb these minerals from the diet (DeLuca, 1988). When dietary calcium intake is inadequate to satisfy the body's calcium requirement, 1,25(OH)2D, along with PTH, mobilizes calcium stores from the bone. In the kidney, 1,25(OH)2D increases calcium reabsorption by the distal renal tubules. Apart from these traditional calcium-related actions, 1,25(OH)2D and its synthetic analogs are increasingly recognized for their potent antiproliferative, prodifferentiative, and immunomodulatory activities (Nagpal et at., 2005).

### 1.35Calcitriol

Calcitriol is known as the active "hormonal" form of vitamin D because

- It stimulates calcium absorption more rapidly than other forms of vitamin D.
- It is more active on a molar basis than any other form.
- It is produced in kidney in a regulated fashion, based on the need for calcium and/or phosphate.
- It has specific receptors in intestine, bone and kidney. It chemically resembles the steroid hormones (Nagpal et at., 2005).
- Absorption and Excretion of vitamin D
- Both vitamins D2 and D3 are absorbed from the small intestine, although vitamin D3 may be absorbed more efficiently. Most of the vitamin appears first within chylomicrons in lymph. Bile is essential for adequate absorption of vitamin D; deoxycholic acid is the major constituent of bile in this regard. The primary route of vitamin D excretion is the bile; only a small percentage is found in the urine. Patients who have intestinal bypass surgery or otherwise have severe shortening or inflammation of the small intestine may fail to absorb vitamin D sufficiently to maintain normal levels; hepatic or biliary dysfunction also may seriously impair vitamin D absorption. Absorbed vitamin D circulates in the blood in association with vitamin D-binding protein, a specific globulin. The vitamin disappears from plasma with a half-life of 19 to 25 hours but is stored in fat depots for prolonged periods (Goodman and Gillman, 2002).

- **Regulation of Calcitriol Production**

Calcitriol, the active form of vitamin D, is an important player in calcium and bone metabolism, but it also has a physiological role beyond its well-known role in skeletal homeostasis. Receptors for Calcitriol are present in various immune cells, including monocytes, macrophages and dendritic cells, as well as T and B lymphocytes, thus suggesting a role for Calcitriol in both innate and adaptive immune responses. Besides being targets, immune cells express vitamin Dactivating enzymes, allowing local

conversion of inactive vitamin D into Calcitriol within the immune system. Data from epidemiological studies are clear: vitamin D deficiency, especially in early life, increases the risk of autoimmune diseases later on and is associated overall with an increased risk of infections. Moreover, higher levels of Calcitriol are associated with relative protection against infections and autoimmune diseases. These association data are corroborated by experiments in preclinical animal models, where data exist that even supplementing with high doses of vitamin D or analogues of Calcitriol can interfere with the course of immune diseases, especially autoimmune diseases like colitis, multiple sclerosis and type 1 diabetes.

Vitamin D without a subscript represents either D2 or D3 or both and is biologically inert. Vitamin D from the skin or diet is only short-lived in circulation (with a half-life of 1–2 days), as it is either stored in fat cells or metabolized in the liver (Mawer et al., 1972). In circulation, vitamin D is bound to vitamin D-binding protein and transported to the liver, where it is converted to 25-hydroxyvitamin D (DeLuca 1984). This majorcirculating form of vitamin D is a good reflection of cumulative effects of exposure to sunlight and dietary intake of vitamin D (Haddad 1973) and is therefore used by clinicians to determine vitamin D status.

**1.36 Vitamin D Reinvented:**

An important clue to roles of vitamin D beyond calcium homeostasis came with the finding that the 1,25-dihydroxyvitamin D nuclear receptor is present in most tissues. A reevaluation of the physiological and pharmacological actions of vitamin D produced evidence that vitamin D can regulate the immune system and thereby is implicated in several immune-mediated diseases. In addition the literature contains reports that vitamin D insufficiency may play a role in the development of multiple sclerosis, rheumatoid arthritis, and asthma, and increases the risk of tuberculosis, pneumonia, poor cognitive function, periodontal disease, and reduced muscle tone and lower-extremity function. (Holick 1995)

Several vitamin D supplementation studies have been reported, especially related to individual cancer types, and most show a modest positive effect. However, the most striking recent study based on vitamin D supplementation is the meta analysis of randomized control trials looking at total mortality .The authors identified 18 such trials of vitamin D intake that reported results for total mortality and found a 7% reduction in total mortality from any cause for patients, most taking relatively modest supplements of vitamin D (400–800 IU/day), compared to controls (Department of Clinical Biochemistry, Glasgow G4 OSF, United Kingdom).

### 1.37 Disorders of Vitamin D

#### 1.37.1 Hypervitaminosis D

The acute or long-term administration of excessive amounts of vitamin D or enhanced responsiveness to normal amounts of the vitamin leads to derangements in calcium metabolism. The responses to vitamin D reflect endogenous vitamin D production, tissue reactivity, and vitamin D intake. Some infants may be hyper reactive to small doses of vitamin D. In adults, hypervitaminosis D results from overtreatment of hypoparathyroidism or secondary hyperparathyroidism of renal osteodystrophy and from faddist use of excessive doses. Toxicity in children also may occur following accidental ingestion of adult doses.

The amount of vitamin D necessary to cause hypervitaminosis varies widely. As a rough approximation, continued daily ingestion of 50,000 units or more by a person with normal

parathyroid function and sensitivity to vitamin D may result in poisoning. Hypervitaminosis D is particularly dangerous in patients who are receiving digoxin because the toxic effects of the cardiac glycosides are enhanced by hypercalcemia.

The initial signs and symptoms of vitamin D toxicity are those associated with hypercalcemia. Since hypercalcemia in vitamin D intoxication generally is due to very high circulating levels of 25-OHD, the plasma concentrations of PTH and Calcitriol typically (but not uniformly) are suppressed. In children, a single episode of moderately severe hypercalcemia may arrest growth completely for 6 months or more, and the

deficit in height may never be fully corrected. Vitamin D toxicity in the fetus is associated with excess maternal vitamin D intake or extreme sensitivity and may result in congenital supravalvular aortic stenosis. In infants, this anomaly frequently is associated with other stigmata of hypercalcemia**.**

### 1.37.2 Hypevitaminosis D

Vitamin D deficiency results in inadequate absorption of Calcium and phosphate. The consequent decrease of plasma Calcium concentration stimulates parathyroid hormone secretion, which acts to restore plasma Calcium at the expense of bone. Plasma concentrations of phosphate remain subnormal because of the phosphaturic effect of increased circulating parathyroid hormone. In children, the result is a failure to mineralize newly formed bone and cartilage matrix, causing the defect in growth known as rickets. As a consequence of inadequate calcification, bones of individuals with rickets are soft, and the stress of weight bearing gives rise to bowing of the long bones.

In adults, vitamin D deficiency results in osteomalacia, a disease characterized by generalized accumulation of undermineralized bone matrix. Severe osteomalacia may be associated with extreme bone pain and tenderness. Muscle weakness, particularly of large proximal muscles, is typical and may reflect both hypophosphatemia and inadequate vitamin D action on muscle. Gross deformity of bone occurs only in advanced stages of the disease. Circulating 25-OHD concentrations below 8 ng/ml are highly predictive of osteomalacia.

### 1.37.3 Hypophosphatemic vitamin D-resistant rickets

In its most common form, is an X-linked disorder of calcium and phosphate metabolism. Calcitriol levels are inappropriately normal for the observed degree of hypophosphatemia. Patients experience clinical improvement when treated with large doses of vitamin D, usually in combination with inorganic phosphate. Even with vitamin D treatment, calcitriol concentrations may remain lower than expected. The genetic basis for Xlinked disorder has been defined (HYP Consortium, 1995). The affected protein, a phosphate-regulating gene with homologies to endopeptidases on the X chromosome is a neutral endoprotease. The substrate for this enzyme likely is involved

in renal phosphate transport. Syndromes closely related to XLH, in which phosphate levels are altered without significant net changes in serum concentrations of calcium, PTH, or 1,25(OH)2D3, include hereditary hypophosphatemic rickets with hypercalciuriaand autosomal dominant hypophosphatemic rickets. The latter disorder maps to chromosome 12p13.3 and is associated with mutations in the gene encoding fibroblast growth factor 23 (Econs et al., 1997)

- Vitamin D-dependent rickets (also called vitamin D-dependent rickets type I)

Is an autosomal recessive disease caused by an inborn error of vitamin D metabolism involving defective conversion of 25-OHD to calcitriol owing to mutations in CYP1□ (1□-hydroxylase). The condition responds to physiological doses of calcitriol (White et al., 2001).

- Hereditary 1,25-dihydroxyvitamin D resistance (also called vitamin D-dependent rickets type II)

Is an autosomal recessive disorder that is characterized by hypocalcemia, osteomalacia, rickets, and total alopecia. Mutations of the vitamin D receptor cause vitamin D-dependent rickets type II (Malloy et al., 1999). Absolute hormone resistance results from premature stop mutations or missense mutations in the zinc finger DNA-binding domain. Several missense mutations in the ligand-binding domain also have been described that result in partial or complete hormone

resistance. These mutations alter ligand binding or heterodimerization with the retinoid X receptor (RXR).

The 25(OH)-vitamin D values are normal, whereas 1,25(OH)2-vitamin D levels are elevated in type II vitamin D-dependent rickets. This clinical feature distinguishes hereditary vitamin Ddependent rickets type II from CYP1deficiency (vitamin D-dependent rickets type I), where serum 1,25(OH)2-vitamin D values are depressed. Children affected by vitamin D-dependent rickets type II are refractory even to massive doses of vitamin D and calcitriol, and they may require prolonged treatment with parenteral Calcium. Some remission of symptoms has been observed during adolescence, but the basis of remission is unknown.

Renal osteodystrophy (renal rickets) is associated with chronic renal failure and is characterized by decreased conversion of 25-OHD to calcitriol. Phosphate retention decreases plasma Calcium concentrations, leading to secondary hyperparathyroidism. In addition, calcitriol deficiency impairs intestinal Calcium absorption and mobilization from bone. Hypocalcemia commonly results (although in some patients, prolonged and severe hyperparathyroidism eventually may lead to hypercalcemia). Aluminum deposition in bone also may play a role in the genesis of the skeletal disease (Goodman and Gillman, 2002).

### 1.38 Minimum Dose of Vitamin D

Naturalness 'In the wide world of supplements, vitamin D is the superstar. For the last few years, this humble nutrient has been featured prominently in allopathic and alternative circles alike. It has basked in the rays of media publicity, and has survived an onslaught of scientific scrutiny. And while such widespread publicity is often good cause for skepticism in the realm of health and medicine, vitamin D appears to be the real deal. Whether we`re talking about heart disease, cancer, diabetes, multiple sclerosis, or Alzheimer`s disease, the "sunshine vitamin" delivers benefits unseen before our time.

### 1.39 Factors affect vitamin D status

- **Sun Exposure**

Catching some rays each day is definitely desirable, and healthy young people can usually get the vitamin D they need from around 10 to 30 minutes of sun exposure per day - depending on their location and the time of year. Most adults in today`s modern world, however, do not even attempt to get this much sun exposure - much less achieve it. Location: Vitamin D is produced in the skin from a cholesterol derivative when we are exposed to UVB radiation from the sun. However, because of the axial tilt of the earth, the further north one lives, the less the sun`s UV B rays will be able to activate vitamin D in the skin. So sun exposure does not necessarily equal optimal vitamin D status if you`re living in the wrong location. Living down south is better, of course but there is still more to consider.

- **Age**

Say we do live close to the equator, or are significantly below the 35 N latitude line. That`s a good thing, and it probably helps. If around 35-40 years old or above, however, we`re likely losing the ability to activate sufficient levels of vitamin D in your skin, even in the unlikely event that we`re getting adequate UVB sun exposure .

- **Dark Skin:**

If we have a lot of pigment in your skin, this is going to shield from the UVB radiation we need, and our probably deficient in vitamin D.

- **Weight:**

Vitamin D requirements are also relative to body weight. If overweight, our body requires more vitamin D than if we are not overweight.

- **Chronic Illness:**

The body demands more vitamin D when we`re sick, and is probably using it up faster than we can get it from the sun.

- **Kind of Supplements should use**

In order to achieve consistent and predictable results, it is important to use the proper carrier form of vitamin D supplements. The absolute best form is an oil-based vitamin D preparation. Dry preparations, like tablets and capsules, should be avoided. Vitamin D is fat soluble, and needs to be taken with fat in order to be properly absorbed - hence the oil-based recommendation. There are two common types of vitamin D: Vitamin D3 (cholecalciferol) and Vitamin D2 (ergocalciferol). Will need to avoid supplementing with vitamin D2 which is a synthetic product made by exposing certain plants to ultraviolet radiation. D2 is not what the human body naturally uses, and compared to D3 it falls far short in terms of efficacy.

### 1.40 Our Body Uses Vitamin D

Vitamin D is a fat-soluble vitamin that promotes absorption of calcium and phosphorus. Most people associate the nutrient calcium with healthy bones and teeth, but no matter how much calcium we have in your diet, without vitamin D, our body can't absorb and use the mineral. So vitamin D is vital for building — and holding — strong bones and teeth.

Researchers at the Bone Metabolism Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston say vitamin D may also reduce the risk of tooth loss by preventing the inflammatory response that leads to periodontal disease, a condition that destroys the thin tissue (ligaments) that connects the teeth to the surrounding jawbone.

Vitamin D comes in three forms: calciferol, cholecalciferol, and ergocalciferol. Calciferol occurs naturally in fish oils and egg yolk. In the United States, it's added to margarines and milk. Cholecalciferzl is created when sunlight hits our skin and ultraviolet rays react with steroid chemicals in body fat just underneath. Ergocalciferol is synthesized in plants exposed to sunlight. Cholecalciferol and ergocalciferol justify vitamin D's nickname: the Sunshine Vitamin.

### 1.41 Vitamin D Deficiency

Vitamin D deficiency is characterized by inadequate mineralization or by demineralization of the skeleton. Among children, vitamin D deficiency is a common cause of bone deformities known as rickets. Vitamin D deficiency in adults leads to a mineralization defect in the skeleton, causing osteomalacia, and induces secondary hyperparathyroidism with consequent bone loss and osteoporosis. Potential roles for vitamin D beyond bone health, such as effects on muscle strength, the risk for cancer and for type 2 diabetes, are currently being studied. The Agency for Healthcare Research and Quality recently reviewed the effectiveness and safety of vitamin D on outcomes related to bone health (Cranney et al, 2007).

### 1.41.1 Risk factors for vitamin D deficiency include:

• Black & ethnic minority patients with darker skin

• Elderly patients in residential care, housebound or institutionalised patients

• Older people aged 65 years and over

• Infants and young children under 5 years of age

• Intestinal malabsorption e.g. coeliac disease, crohns disease, gastrectomy, cholestatic liver disease

• Routine covering of face or body e.g. habitual sunscreen use factor 15 or above

• Vegan/vegetarian diet

• Liver or renal disease

• Medications including certain anticonvulsants, cholestyramine, colestipol, liquid paraffin,

sucralfate, rifampicin, glucocorticoids, highly active antiretrovirals

• Obesity (BMI >30)

• All pregnant and breast feeding women, especially teenagers and young women

• Short interval pregnancies

• Patients with persistently low calcium, low phosphate or raised Alkaline Phosphatase

• Low vitamin D dietary intake

• Cystic fibrosis

• If one family member is Vitamin D deficient it is likely others in the family may also be deficient, unless that person has a specific medical condition

**1.42 Research indicates vitamin D deficiency is a causal factor in all facets of human health, as shown below (Sievenpiper et al, 2008 ).**

**Brain and Mind**

- Alzheimer's
- AnxietyAutism
- Brain birth-defects
- Dementia
- Depression
- Insomnia
- Multiple Sclerosis
- Fatigue and malaise
- Parkinson's
- Insomnia
- Irritability
- Reduced IQ
- Schizophrenia
- Psychosis

**Body**

- ✓ Aneurysm
- ✓ Arthritis and pain
- ✓ Asthma
- ✓ Chronic pain
- ✓ Diabetes
- ✓ Fibromyalgia
- ✓ Heart disease
- ✓ Hypertension
- ✓ Hip fractures
- ✓ Hypothyroid
- ✓ Hemorrhoids

- ✓ Migraines
- ✓ Multiple sclerosis
- ✓ Muscle weakness
- ✓ Muscle wasting
- ✓ Osteoarthritis
- ✓ Osteoporosis
- ✓ Periodontal disease
- ✓ Rickets
- ✓ Seizure
- ✓ Stroke

### 1.43 Immune System of human body

#### 1.43.1 Varieties of cancer Common colds Common flues & H1N1

Once foods were fortified with vitamin d and rickets appeared to have been conquered, many health care professionals thought the majorhealth problems resulting from vitamin D deficiency had been resolved. However,rickets can be considered the tip of the vitamin D–deficiency iceberg. In fact, vitamin D deficiency remains common in children and adults. In uteri and during childhood, vitamin D deficiency can cause growth retardation and skeletal deformities and may increase the risk of hip fracture later in life. Vitamin D deficiency in adults can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalaciaandmuscle weakness, and increase the risk of fracture.The discovery that most tissues and cells in the body have a vitamin D

receptor and that several possess the enzymatic machinery to convert the primary circulating form of vitamin D, 25-hydroxyvitamin D, to the active form, 1,25-dihydroxyvitamin D, has provided new insights into the function of this vitamin. Of great interest is the role it can play in decreasing the risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease. (Pearce and Cheetham, 2010)

### 1.43.2 Cancer

People living at higher latitudes are at increased risk for Hodgkin's lymphoma as well as colon, pancreatic,prostate, ovarian, breast, and other cancers and are more likely to die from these cancers, as compared with people living at lower latitudes.55‑65Both prospective and retrospective epidemiologic studies indicate that levels of 25-hydroxyvitamin D below 20 mg per milliliter are associated with a30 to 50% increased risk of incident colon, prostate, and breast cancer, along with higher mortality from these cancers. (Holick,2004 )

### 1.43.3 Autoimmune Diseases, Osteoarthritis, and Diabetes

Living at higher latitudes increases the risk of type 1 diabetes, multiple sclerosis, and Crown's disease.68,69 Living below 35 degrees latitude for the first 10 years of life reduces the risk of multiple sclerosis by approximately 50%.69,70 Among white men and women, the risk of multiple sclerosis decreased by 41% for every increase of 20 ng per milliliter in 25hydroxyvitamin D above approximately24 mg per milliliter(60 mol per liter) Women who ingested more than 400 IU of vitamin D per day had a 42% reduced risk of developing multiple sclerosis.72 Similar observations have been made for rheumatoid arthritis73 and osteoarthritis.74 Several studies suggest that vitamin D supplementation in children reduces the risk of type

1diabetes. Increasing vitamin D intake during pregnancy reduces the development of islet auto antibodies in offspring.53 For 10,366 children in Finland who were given 2000 IU of vitamin D3 per day during their first year of life and were followed for 31 years, the risk of type 1 diabetes was reduced by approximately 80%.75 Among children with vitamin D deficiency the risk was increased by approximately 200%. In another study, vitamin D deficiency increased insulin resistance, decreased insulin production, and was associated with the metabolic syndrome.53 Another study showed that a combined daily intake of 1200 mg of calcium and 800 IU of vitamin D lowered the risk of type 2 diabetes by 33% 0.90) as compared with a daily intake of less than 600 mg of calcium and less than 400 IU of vitamin D. (Holick,2004 )

### 1.43.4 Cardiovascular Disease

Living at higher latitudes increases the risk of hypertension and cardiovascular disease.54,77 In a study of patients with hypertension who were exposed to ultraviolet B radiation three times a week for 3 months, 25-hydroxyvitamin D levels increased by approximately 180%, and blood pressure became normal (both systolic and diastolic blood pressure reduced by 6 mm Hg).78 Vitamin D deficiency is associated with congestive heart failure54 and blood levels of inflammatory factors, including C-reactive protein and interleukin-10.54,79 Vitamin D Deficiency and Other Disorders. (Holick, 2004)

### 1.43.5 Schizophrenia and Depression

Vitamin D deficiency has been linked to an increased incidence of schizophrenia and depression. 80,81 Maintaining vitamin D sufficiency in uteri and during early life, to satisfy the vitamin D receptor transcriptional activity in the brain, may be important for brain development as well as for maintenance of mental function later in life**.**

### 1.43.6 Lung Function and Wheezing Illnesses

Men and women with a 25-hydroxyvitamin D level above 35 ng per milliliter (87 mol per liter) had the Children of women living in an inner city who had vitamin D deficiency during pregnancy are at increased risk for wheezing illnesses.

### 1.43.7 Mal absorption and Medication of vitamin D

Patients with mild or moderate hepatic failure or intestinal fat-mal absorption syndromes, as well as patients who are taking anticonvulsant medications, glucocorticoids, or other drugs that

activate steroid and xenobiotic receptor, require higher doses of vitamin D .Exposure to sunlight or ultraviolet B radiation from a tanning bed or other ultraviolet B–emitting device is also effective. Sunlight and Artificial Ultraviolet B Radiation Sensible sun exposure can provide an adequate amount of vitamin D3, which is stored in body fat and released during the winter.

### 1.44 Vitamin D Toxicity

Too much vitamin D can be harmful, it certainly can - though anything can be toxic in excess, even water. As one of the safest substances known to man, vitamin D toxicity is very rare. In fact, people are at far greater risk of vitamin D deficiency than they are of vitamin D toxicity. Vitamin D toxicity is a condition where blood serum concentrations of vitamin D's storage form, calcidiol, become too high, causing adverse systemic effects**.**

- **Toxic doses of vitamin D**

What exactly constitutes a toxic dose of vitamin D has yet to be determined, though it is possible this amount may vary with the individual. Published cases of toxicity, for which serum levels and dose are known, all involve intake of ≥ 40000 IU (1000 mcg) per day. Two different cases involved intake of over 2,000,000 IU per day - both men survived.

- **Serum levels of vitamin D**

Upper limit and toxicity threshold Upper limit for a substance is the amount up to which is considered safe and without risk of adverse effects in the majority of the population. Toxicity threshold for a substance is the amount beyond which over-saturation occurs and symptoms of toxicity manifest. These values for calcitriol are as follows: Toxicity threshold level - 200-250 mg/mol (500-750 mol/L) Upper limit - 100 mg/mL (250 mol/L)

### 1.45 Symptoms: toxicity and overdose

- **Signs of vitamin D toxicity are high urine and blood calcium**

The first sign of vitamin D toxicity is hypercalciuria (excess calcimine the urine) followed by hypercalcemia (high bloodcalcium). The following symptoms may present :

- vomiting
- poor appetite
- constipation (possibly alternating with diarrhea)
- weakness
- weight loss
- tingling sensations in the mouth

- confusion
- heart rhythm abnormalities
- the immediate symptoms of vitamin D overdose are:
  - ✓ abdominal cramps
  - ✓ nausea and vomiting It is fairly difficult to become toxic using vitamin D3. If we think we may be toxic because we are having an adverse reaction to vitamin D but we have not been using excessive amounts like those described above, or symptoms could be due to reasons other than toxicity. If the results show a serum calcitriol level of 200-250 ng/mol (500-750 mol/L) or more, it could be toxic.
- the following measures should be taken until vitamin D levels return to normal:

✓ avoidance of direct sunlight exposure
✓ avoidance of foods and supplements containing vitamin D
✓ restriction of calcium intake
✓ drinking 8 glasses of water daily In most cases, vitamin D toxicity can be corrected without lasting problems, provided the body has not remained in a hypercalcemia state for too long. Hypocalcaemia has the potential to cause soft tissue calcification, resulting in deposits of calcium crystals in the heart, lungs, and/or kidneys. With prolonged hypercalcemia, permanent damage is possible if calcification is severe enough.

**1.46 Use of Vitamin D in the Regulation of Calcium, Phosphorus, and Bone Metabolism**

During exposure to solar ultraviolet B (UVB) radiation, 7-dehydrocholesterol in the skin is converted to previtamin D3, which is immediately converted to vitamin D3 in a heat-dependent process. Excessive exposure to sunlight degrades previtamin D3 and vitamin D3 intoInactive photoproducts. Vitamin D2 and vitamin D3 from dietary sources are incorporated into chylomicrons and transported by the lymphatic system into the venous circulation. Vitamin D made in the skin or ingested in the diet can be stored in and then released from fat cells. Vitamin D in the circulation is bound to the vitamin D–binding protein, which transports it to the liver, where vitamin D is converted by vitamin

D-25- hydroxylase to25-hydroxyvitamin D. This is the major circulating form of vitamin D that is used by clinicians to determine vitamin D status.

### 1.46.1 Analogs of Calcitriol

Several vitamin D analogs suppress parathyroid hormone secretion by the parathyroid glands but have less or negligible hypercalcemic activity. They therefore offer a safer and more effective means of controlling secondary hyperparathyroidism.

Calcipotriol (calcipotriene) is a synthetic derivative of calcitriol with a modified side chain that contains a 22-23 double bond, a 24(S)-hydroxy functional group, and carbons 25 to 27 incorporated into a cyclopropane ring. Calcipotriol has comparable affinity with calcitriol for the vitamin D receptor, but it is less than 1% as active as calcitriol in regulating calcium metabolism. This reduced calcemic activity largely reflects the pharmacokinetics of calcipotriol (Kissmeyer and Binderup, 1991). Calcipotriol has been studied extensively as a treatment for psoriasis (see Chapter 62), although its mode of action is not known; a topical preparation (DOVONEX) is available for that purpose. In clinical trials, topical calcipotriol has been found to be slightly more effective than glucocorticoids with a good safety profile.

Paricalcitol (1,25-dihydroxy-19-norvitamin D2, ZEMPLAR) is a synthetic calcitriol derivative that lacks the exocyclic C19 and has a vitamin D2 rather than vitamin D3 side chain. It reduces serum parathyroid hormone levels without producing hypercalcemia or altering serum phosphorus (Martin et al., 1998). In an animal model, paricalcitol prevented or reversed parathyroid hormone induced high-turnover bone disease (Slatopolsky et al., 2003). Paricalcitol administered intravenously is FDA approved for treating secondary hyperparathyroidism in patients with chronic renal failure.

22-Oxacalcitriol (1,25-dihydroxy-22-oxavitamin D3, OCT, maxicalcitol, OXAROL) differs from calcitriol only in the substitution of C-22 with an oxygen atom. Oxacalcitriol has a low affinity for vitamin D-binding protein; as a result, more of the drug circulates in the free (unbound) form, allowing it to be metabolized more rapidly than calcitriol with a consequent shorter half-life. Oxacalcitriol is a potent suppressor of parathyroid hormone gene expression and shows very limited activity on intestine and bone. It is a useful

compound in patients with overproduction of parathyroid hormone in chronic renal failure or even with primary hyperparathyroidism (Cunningham, 2004).

### 1.46.2 Indications for Therapy with Vitamin D

The major therapeutic uses of vitamin D may be divided into four categories: (1) prophylaxis and cure of nutritional rickets; (2) treatment of metabolic rickets and osteomalacia, particularly in the setting of chronic renal failure; (3) treatment of hypoparathyroidism; and (4) prevention and treatment of osteoporosis.

### 1.46.3 Nutritional Rickets

Nutritional rickets results from inadequate exposure to sunlight or deficiency of dietary vitamin D. The condition, once extremely rare in the United States and other countries where food fortification with the vitamin is practiced, is now increasing. Infants and children receiving adequate amounts of vitamin D-fortified food do not require additional vitamin D; however, breast-fed infants or those fed unfortified formula should receive 400 units of vitamin D daily as a supplement. The usual practice is to administer vitamin A in combination with vitamin D. A number of balanced vitamin A and D preparations are available for this purpose. Since the fetus acquires more than 85% of its calcium stores during the third trimester, premature infants are especially susceptible to rickets and may require supplemental vitamin D.

Treatment of fully developed rickets requires a larger dose of vitamin D than that used prophylactically. One thousand units daily will normalize plasma Calcium and phosphate concentrations in approximately 10 days, with radiographic evidence of healing within about 3 weeks. However, a larger dose of 3000 to 4000 units daily often is prescribed for more rapid healing, particularly when respiration is compromised by severe thoracic rickets.

Vitamin D may be given prophylactically in conditions that impair its absorption (e.g., diarrhea, steatorrhea, and biliary obstruction). Parenteral administration also may be used in such cases.

### 1.46.4 Treatment of Osteomalacia and Renal Osteodystrophy

Osteomalacia, distinguished by undermineralization of bone matrix, occurs commonly during sustained phosphate depletion. Patients with chronic renal disease are at risk for developing osteomalacia but also may develop a complex bone disease called renal osteodystrophy. In this setting, bone metabolism is stimulated by an increase in parathyroid hormone and by a delay in bone mineralization that is due to decreased renal synthesis of calcitriol. In renal osteodystrophy, low bone mineral density may be accompanied by high-turnover bone lesions typically seen in patients with uncontrolled hyperparathyroidism or by low bone remodeling activity seen in patients with adynamic bone disease. The therapeutic approach to the patient with renal osteodystrophy depends on its specific type. In high-turnover (hyperparathyroid) or mixed highturnover disease with deficient mineralization, dietary phosphate restriction, generally in combination with a phosphate binder, is recommended because phosphate restriction is limited by the need to provide adequate protein intake to maintain nitrogen balance. Although highly effective, aluminum is no longer used as a phosphate binder because it promotes adynamic bone disease, anemia, myopathy, and occasionally dementia. Calcium-containing phosphate binders along with calcitriol administration may contribute to oversuppression of parathyroid hormone secretion and likewise result in adynamic bone disease and an increased incidence of vascular calcification. Highly effective non-calcium-containing phosphate binders have been developed. Sevelamer hydrochloride (RENAGEL), a nonabsorbable phosphate-binding polymer, effectively lowers serum phosphate concentration in hemodialysis patients, with a corresponding reduction in the calcium phosphate product. Sevelamer hydrochloride consists of cross-linked poly[allylaminehydrochloride] that is resistant to digestive degradation. Partially protonated amines spaced one carbon from the polymer backbone chelate phosphate ions by ionic and hydrogen bonding. Side effects of sevelamer include vomiting, nausea, diarrhea, and dyspepsia. Sevelamer does not affect the bioavailability of digoxin, warfarin, enalapril, or metoprolol. (Monier-Faugere et al., 2001) Renal osteodystrophy associated with low bone turnover (adynamic bone disease) is increasingly common and may be due to oversuppression of parathyroid hormone with aggressive use of either calcitriol or other vitamin D analogs. Whileparathyroid hormone

levels generally are low (100 pg/ml), a high parathyroid hormone level does not exclude the presence of adynamic bone disease, especially with parathyroid hormone assays that do not distinguish between biologically active and inactive parathyroid fragments. Current guidelines suggest that treatment with an active vitamin D preparation is indicated if serum levels are less than 30 ng/ml and serum calcium is less than 9.5 mg/dl (2.37 mM). However, if calcitriol and serum calcium levels are elevated, vitamin D supplementation should be discontinued. If the serum calcium level is less than 9.5 mg/dl, treatment with a vitamin D analog is warranted irrespective of the calcitriol level (Eknoyan et al., 2003).

### 1.47 Hypoparathyroidism

Vitamin D and its analogs are a mainstay of the therapy of hypoparathyroidism. Dihydrotachysterol has a faster onset, shorter duration of action, and a greater effect on bone mobilization than does vitamin D and traditionally has been a preferred agent. Calcitriol also is effective in the management of hypoparathyroidism and certain forms of pseudohypoparathyroidism in which endogenous levels of calcitriol are abnormally low. However, most hypoparathyroid patients respond to any form of vitamin D. Calcitriol may be preferred for temporary treatment of hypocalcemia while awaiting effects of a slower-acting form of vitamin D.

### 1.48 Miscellaneous uses of Vitamin D

Vitamin D is used to treat hypophosphatemia associated with Fanconi syndrome. Large doses of vitamin D (over 10,000 units/day) are not useful in patients with osteoporosis and even can be dangerous. However, administration of 400 to 800 units/day of vitamin D to frail, elderly men and women has been shown to suppress bone remodeling, protect bone mass, and reduce fracture incidence. Clinical trials suggest that calcitriol may become an important agent for the treatment of psoriasis. As such nontraditional uses of vitamin D are discovered, it will become important to develop noncalcemic analogs of calcitriol that achieve effects on cellular differentiation without the risk of hypercalcemia (Kowalzick, 2001**).**

### 1.49 Adverse Effects of Vitamin D Therapy

The primary toxicity associated with calcitriol reflects its potent effect to increase intestinal calcium and phosphate absorption, along with the potential to mobilize osseous calcium and phosphate. Hypercalcemia, with or without hyperphosphatemia, commonly complicates calcitriol therapy and may limit its use at doses that effectively suppress parathyroid hormone secretion. As described earlier, noncalcemic vitamin D analogs provide alternative interventions, although they do not obviate the need to monitor serum calcium and phosphorus concentrations.

Hypervitaminosis D is treated by immediate withdrawal of the vitamin, a low-calcium diet, administration of glucocorticoids, and vigorous fluid support. As noted earlier under hypercalcemia, forced saline diuresis with loop diuretics is also useful. With this regimen, the plasma Calcium concentration falls to normal, and Calcium in soft tissue tends to be mobilized. Conspicuous improvement in renal function occurs unless renal damage has been severe. (Goodman and Gillman, 2002)

## Aim of the study

- To aware women about Calcium and Vitamin D
- To aware about the disease that occur due to calcium deficiency
- To aware about Vitamin D deficiency
- Make people conscious about dietery health
- Make people healthy

# Chapter two
# Literature Review

# Literature review

## 2.1 Awareness regarding the importance of calcium and vitamin D among the undergraduate pharmacy students in Bangladesh

Riaz Uddin,corresponding author1 Naz Hasan Huda et al

Calcium and vitamin D are two important micronutrients required for maintaining proper bone health. Previous works intended to determine the status of these micronutrients in local population have reported that the people in Bangladesh are at high risk of calcium insufficiency and hypovitaminosis D related health complications. Lack of awareness and insufficient knowledge of the essentiality of these two nutrients are assumed to cause this problem in Bangladesh. The present study was designed and conducted to establish a basic understanding on the level of gap of knowledge and awareness among pharmacy students at undergraduate level in Bangladesh.A total of 713 students of Bachelor of Pharmacy course participated in the study. The students were asked about basic idea related to calcium and vitamin D and the disorders due to their deficiency, name of common foods containing calcium and vitamin D, their perception regarding the essentiality of the said nutrients etc. It was found that most of the students were familiar with the importance of calcium (98.9%) and vitamin D (99.3%) in bone health. 82.2% students know about the term osteoporosis. Unfortunately, 10.7% and 18.8% students failed to mention at least one food that is rich in calcium and vitamin D, respectively. Most of the students got familiar about the nutrients from their teachers (48.9%) and textbooks (32.8%). (BMC Research Notes, 6(1), p.134.)

## 2.2 Calcium and Vitamin D Related Knowledge in 16-18 Years Old Adolescents: Does Living in Urban or Rural Areas

MatterDewan Taslima Akhter, Riaz Uddin et al

Vitamin D deficiency is very common in Bangladesh. However, there is scanty of literature available about the knowledge of calcium and vitamin D in 16-18 years old adolescents. The present study has been conducted to determine whether a lack of knowledge exists in this age group about these nutrients and to find out the correlation between students' living in urban or rural areas. We conducted a cross sectional survey

in 2992 students living in urban (62.6%) and rural (37.4%) areas aged between 16-18 years. We followed a 2 step sampling technique. 6 colleges from both urban and rural areas were selected by convenience of the interviewers and then required sample size was calculated from the number of students of each college. The students filled up a questionnaire after a detailed briefing about the study by the interviewer.We found that many of the students, both from urban and rural settings have lack of knowledge and awareness of calcium and vitamin D. Our data suggest that though the rural students are less familiar with vitamin D ($p<0.001$) and osteoporosis ($p=0.0056$) than urban students, they exercise a healthy diet in terms of milk consumption ($p<0.0001$) and engage themselves more in outdoor activities, spend more time in sunlight ($p<0.0001$) than the urban students. Thus the rural students may require less supplemental support of calcium and/or vitamin D than the urban students ($p<0.0001$).(Riaz Uddin et al)

### 2.3 Knowledge Regarding Vitamin D Among Private University Students in Malaysia

Audrey Sharmaine A/P Rajaretnam1, Mohammed A Abdalqader et al

Vitamin D is known as the sunlight vitamin which mainly helps in bone metabolism and calcium homeostasis. It is estimated that one billion people have vitamin D deficiency and it is considered as a public health problem. The purpose of this study is to explore the knowledge among students regarding vitamin D and its associated factors. A cross-sectional study was conducted among 360 private university students using self-administered questionnaires regarding vitamin D Knowledge on aspects of vitamin D sources, health benefits, factors of vitamin D deficiency and recommended intakes and some others. Females were more predominant in this study (69.4 %). Most students are aware and have good knowledge regarding vitamin D with male having a higher knowledge compared to female. Besides that, 69% of them agreed that vitamin D main source is the sun. only 11.1 % know the correct answer regarding the recommended daily dosage of vit. D which is 600 IU per day.(Mohammed A Abdalqader et al)

## 2.4 Vitamin D Supplementation Among Women of Childbearing Age: Prevalence and Disparities

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Maternal vitamin D deficiency is associated with numerous adverse health conditions. However, most women of childbearing age are vitamin D deficient. Although scientific and public awareness about vitamin D deficiency's role in health has increased in recent years, current data are not available to assess whether there have been concomitant increases of supplementation among women of childbearing age. We assessed prevalence and significant associations of vitamin D supplementation among childbearing-age women (16–49 years) in the most recently available

Sampling weights were applied to account for the complex survey design and ensure generalizability to women of childbearing age among the noninstitutionalized population in the US. 2 Analyses were conducted using Stata versions 11 and 12 (College Station, TX). Of 1749 women, 459 (33%) had taken supplements containing vitamin D during the past 30 days. We observed low supplementation prevalence (range 12%–27%) among teenagers, those with high body mass index (BMI), low socio-economic status (low-income, low education, ethnicity other than white, food insecurity, or no/government insurance), as well as parous women who had never breastfed, and women with no history of vigorous or moderate exercise. In the fully adjusted regression models, 2 Mexican-American race/ethnic identity (OR: .53, 95% CI .33–.86), low food security (OR: .65, 95% CI .44–.95), no health insurance (OR .65, 95% CI .42–1.00), government/other health insurance (OR: .66, 95% CI .45–.96), and parity without breastfeeding (OR: .63, 95% CI .40–.99) were associated with lower likelihood of vitamin D supplement use compared with the reference groups.(BScN Committee Members: Mario Kratz et al)

# Chapter three
# Methodology

# Methodology

## 3.1 Type of the Study

It was a survey based study.

## 3.2Study Area

East West University,Ahsanullah university of science and technology,Citycollege,Dhaka city.

## 3.3 Study Population

In this study, a total number of 200 girls and women were surveyed with a questionnaire in order to assess the knowledge, perception and attitude regarding awareness of calcium and vitamin D. Informed consent was obtained from the eligible participants before interviewed and participants who agreed to join the study provided the required information for the studies.

## 3.4 Study Period

The duration of the study was about five months starting from January to May in 2016.

## 3.5 Questionnaire Development

The pre-tested questionnaire was specially designed to collect the simple background data and the needed information. The questionnaire was written in simple English in order to avoid unnecessary semantic misunderstanding. The questionnaire was pilot tested to ensure it was understandable by the participants. Extra space was however, allowed after some questions for the participants' comments; and in most cases, these were used as qualifying remarks which aided considerably in giving answers to specific questions and in providing additional information which assisted the interviewers in drawing up conclusions.

### 3.6 Sampling Technique

In this study purposive sampling technique was followed.

### 3.7 Data Analysis

After collecting, the data were checked and analyzed with the help of Microsoft Excel 2010. The result was shown in bar, pie and column chart and calculated the percentage of the knowledge attitude and perception regarding awareness of calcium and vitamin D.

# QUESTIONNAIRE

## Part 1: Personal data

| | | | | |
|---|---|---|---|---|
| **1** | Age: | | | |
| **2** | Do you have child? | □Yes | □No | |
| **3** | Are you suffering from any bone disorder? | □Yes | □No | |
| **4** | Were you ever been prescribed calcium supplement? | □Yes | □No | Reason |
| **5** | Were you ever been prescribed vitamin D? | □Yes | □No | Reason |

## Part 2: Awareness and knowledge regarding calcium and vitamin D :

| | | | |
|---|---|---|---|
| **6** | Do you think calcium is an important mineral? | □Yes | □No |
| **7** | Write 3 sources of Calcium: | | □do not know |
| **8** | Do you agree that Vitamin D is essential for normal physiological function? | □Yes | □No |
| **9** | Write 3 sources of Vitamin D: | | □do not know |
| **10** | From where did you learn about calcium? | □books | □ family |
| | | □ internet | □ teacher |
| | | □ media | □ doctor |
| | | □ others: | |
| **11** | Do you know what should be the | □For women: | □For children: |

| | | | |
|---|---|---|---|
| | daily intake of calcium? | | |
| **12** | Do you know what should be the daily intake of Vitamin D? | □For women: | □For children: |
| **13** | What is osteoporosis? | | □do not know |
| **14** | Do you think women are more affected by osteoporosis than men? | ☐Yes | ☐ No |
| **15** | What diseases do children suffer due to calcium deficiency? | | □do not know |
| **16** | What is the frequency of your child's milk consumption? | □daily | □weekly |
| | | □monthly | □yearly |
| | | □never | □ others: |
| **17** | What is the daily sunlight exposure? | □ less than 1hr | □ greater than 1hr |
| | | □ greater than 2 hr | □greater than 3 hr |
| | | □greater than 4 hr | □ do not know |
| | | □ others | |

# Chapter four
# Result

# Result

## 4.1 Number of respondents who have children

**Table: 4.1 Number of respondents who have children**

| Responded women having children | Yes | No | Total |
|---|---|---|---|
| Number | 127 | 73 | 200 |
| Percentage | 63.50% | 36.50% | |

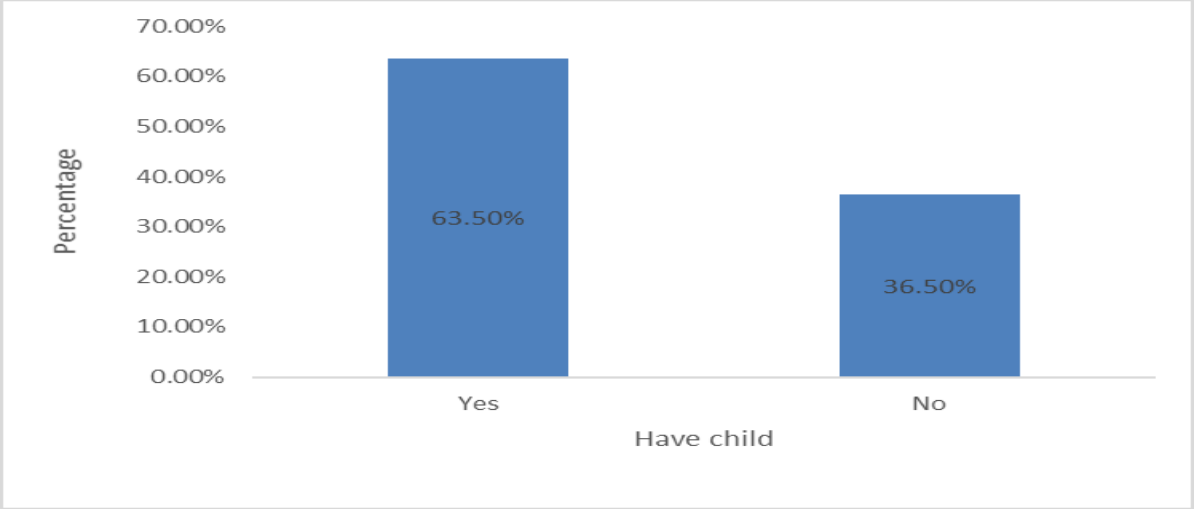



Figure 4.1: Number of respondents who have children

In this study we found that 63.5% women have child and 36.5% women don't have child.

### 4.2 Number of respondents who are suffering from bone disorder

**Table 4.2 Number of respondents who are suffering from bone disorder**

| Number of respondents who are suffering from bone disorder | Yes | No | Total |
|---|---|---|---|
| Number | 64 | 136 | 200 |
| Percentage | 32% | 68% | |

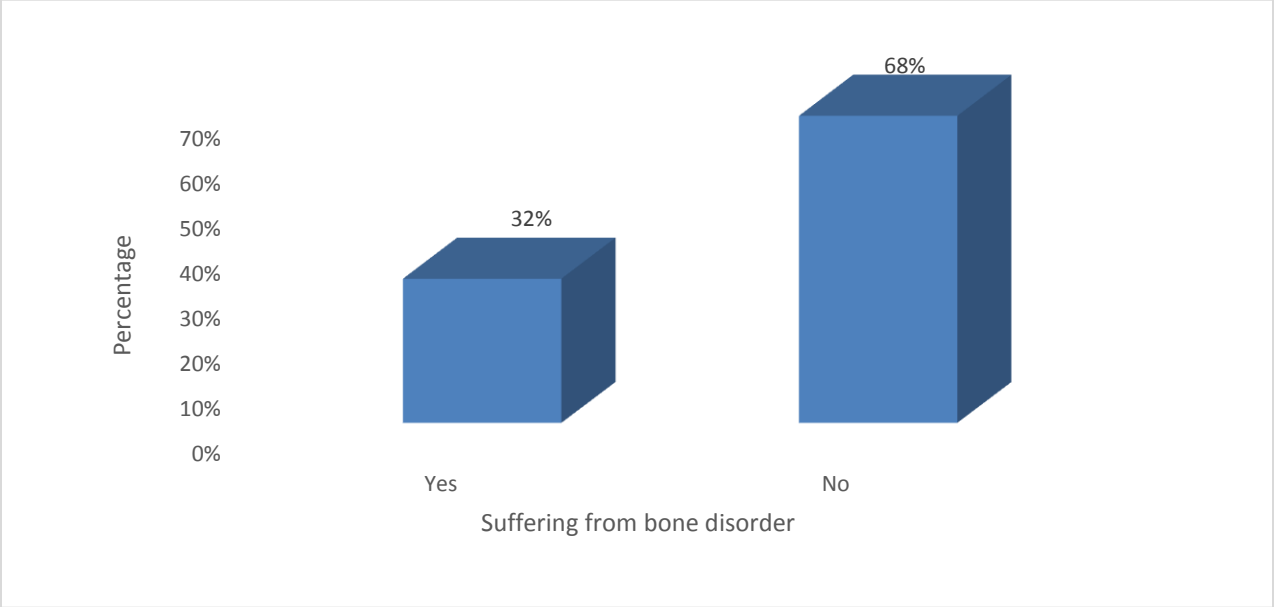



**Figure 4.2: Number of respondents who are suffering from bone disorder**

In this study we see that 32% population are suffering from bone disorder and 68% population are not suffering from bone disorder.

### 4.3 Number of respondents who have been prescribed calcium supplement

**Table 4.3 Number of respondents who have been prescribed calcium supplement**

| Number of respondents who have been prescribed calcium supplement | Yes | No | Total |
|---|---|---|---|
| Number | 77 | 121 | 200 |
| Percentage | 38.5% | 60.5% | |

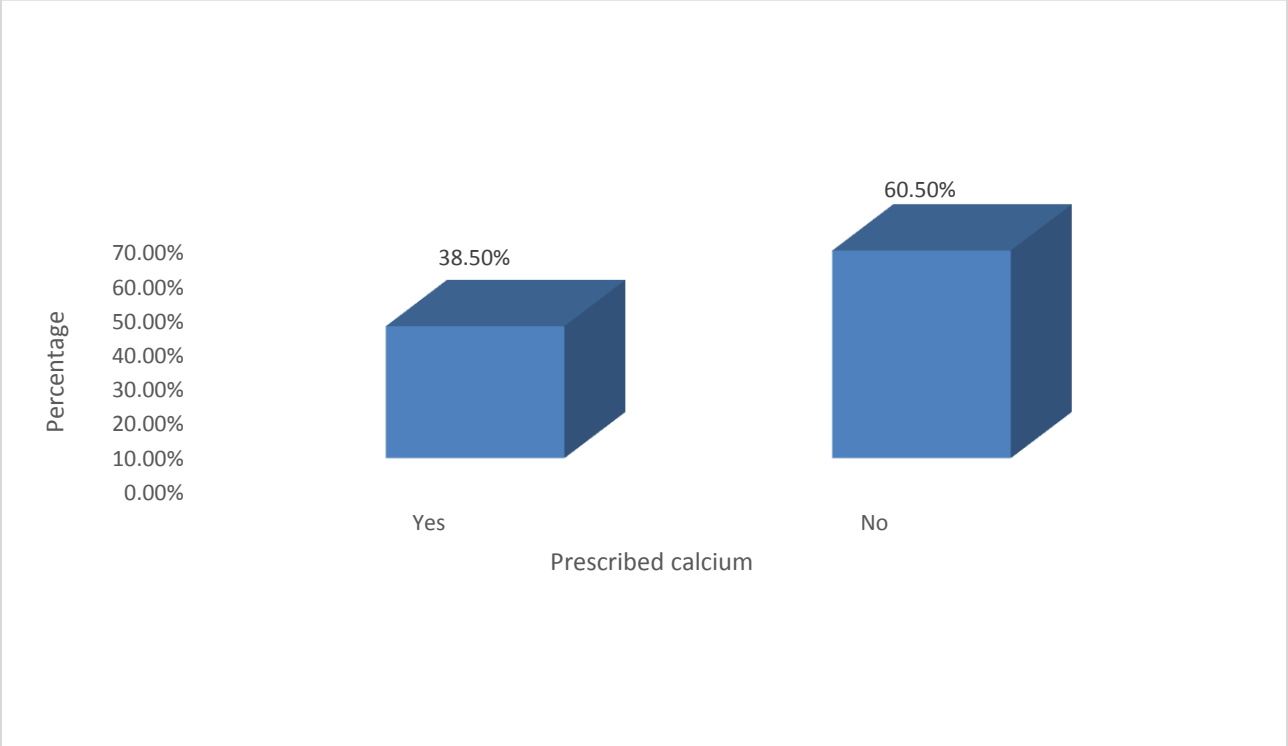



Figure4.3: Number of respondents who have been prescribed calcium supplement

Here, 38.5% women are prescribed calcium supplement and 60.5% women are not prescribed calcium supplement.

### 4.4 Number of respondents who have been prescribed Vitamin D

**Table 4.4 Number of respondents who have been prescribed Vitamin D**

| Number of respondents who have been prescribed Vitamin D | Yes | No | Total |
|---|---|---|---|
| Number | 80 | 121 | 200 |
| Percentage | 40% | 60.5% | |

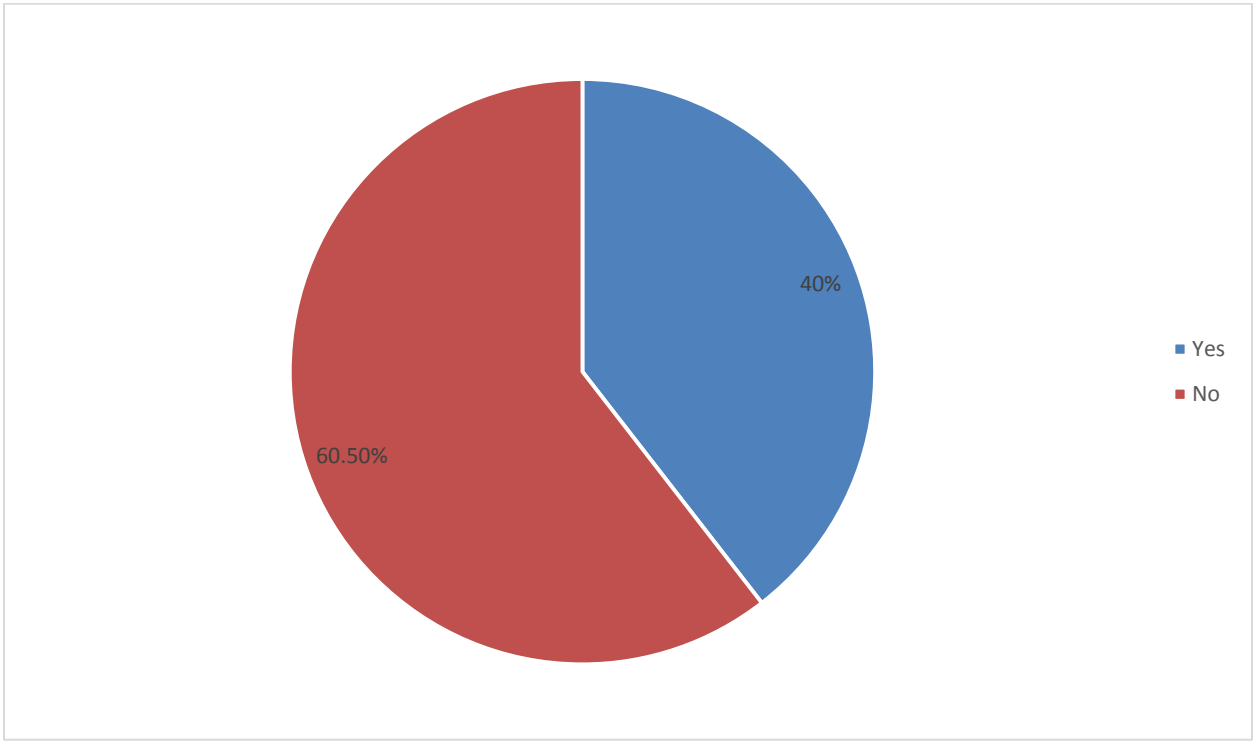



Figure4.4 Number of respondents who have been prescribed Vitamin D

In this study,we found that 40% women are prescribed Vitamin D and 60.5% women are not prescribed Vitamin D.

### 4.5 Respondents asked if calcium is an important mineral

**Table 4.5 Respondents asked if calcium is an important mineral**

| Respondents asked if calcium is an important mineral | Yes | No | Total |
|---|---|---|---|
| Number | 156 | 44 | 200 |
| Percentage | 78% | 22% | |

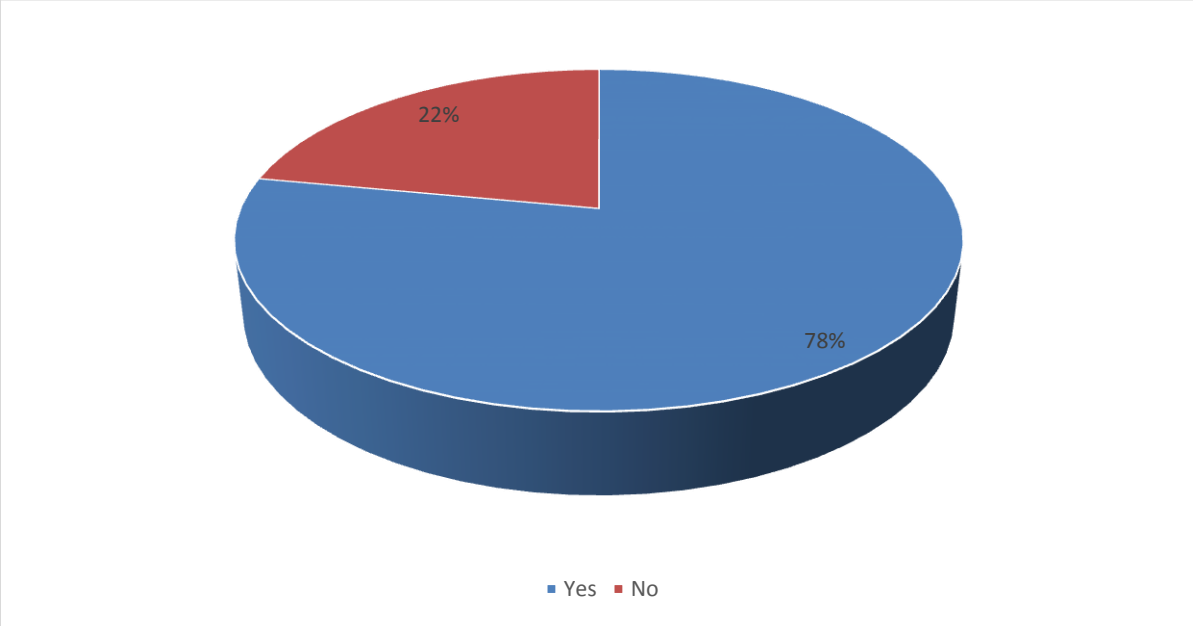



Figure 4.5: Respondents asked if calcium is an important mineral

In this study,we found that 78% people are agree about that calcium is an important mineral and 22% people are not agree with this statement.

### 4.6 Number of respondents who are aware about sources of calcium

**Table 4.6 Number of respondents who are aware about sources of calcium**

| Number of respondents who are aware about sources of calcium | Yes | Do not know | Total |
|---|---|---|---|
| Number | 83 | 117 | 200 |
| Percentage | 41.5% | 58.5% | |

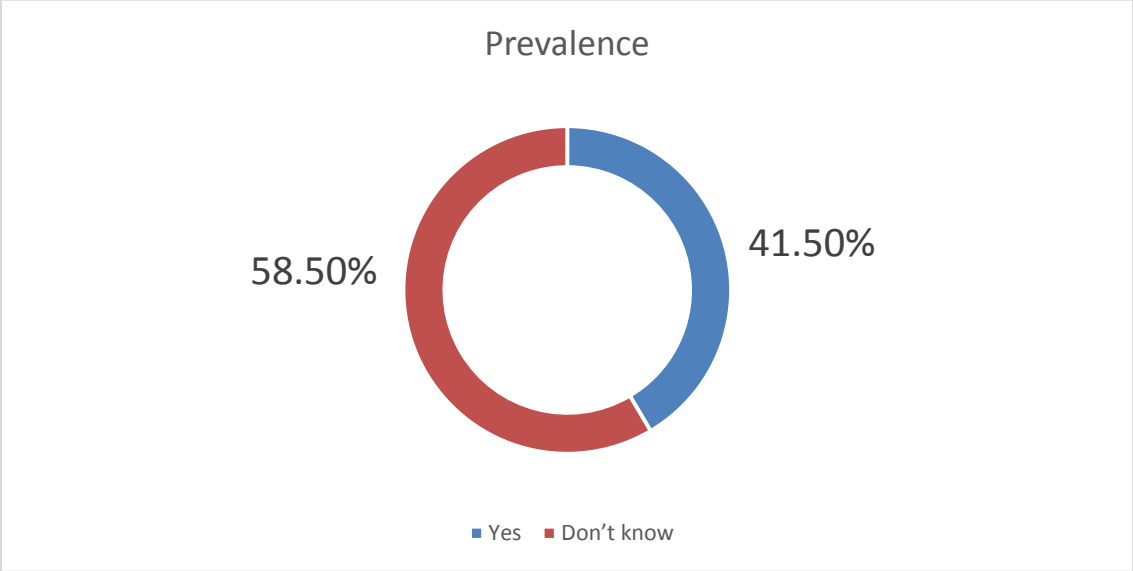



Figure 4.6**:**Number of respondents who are aware about sources of calcium

In this research,we found that 41.50% population knows about the sources of calcium and 58.5% population don't know about the sources.

### 4.7: Number of respondents who are asked if Vitamin D is essential

**Table 4.7 : Number of respondents who are asked if Vitamin D is essential**

| Number of respondents who are asked if Vitamin D is essential | Yes | No | Total |
|---|---|---|---|
| Number | 143 | 56 | 200 |
| Percentage | 71.5% | 28% | |

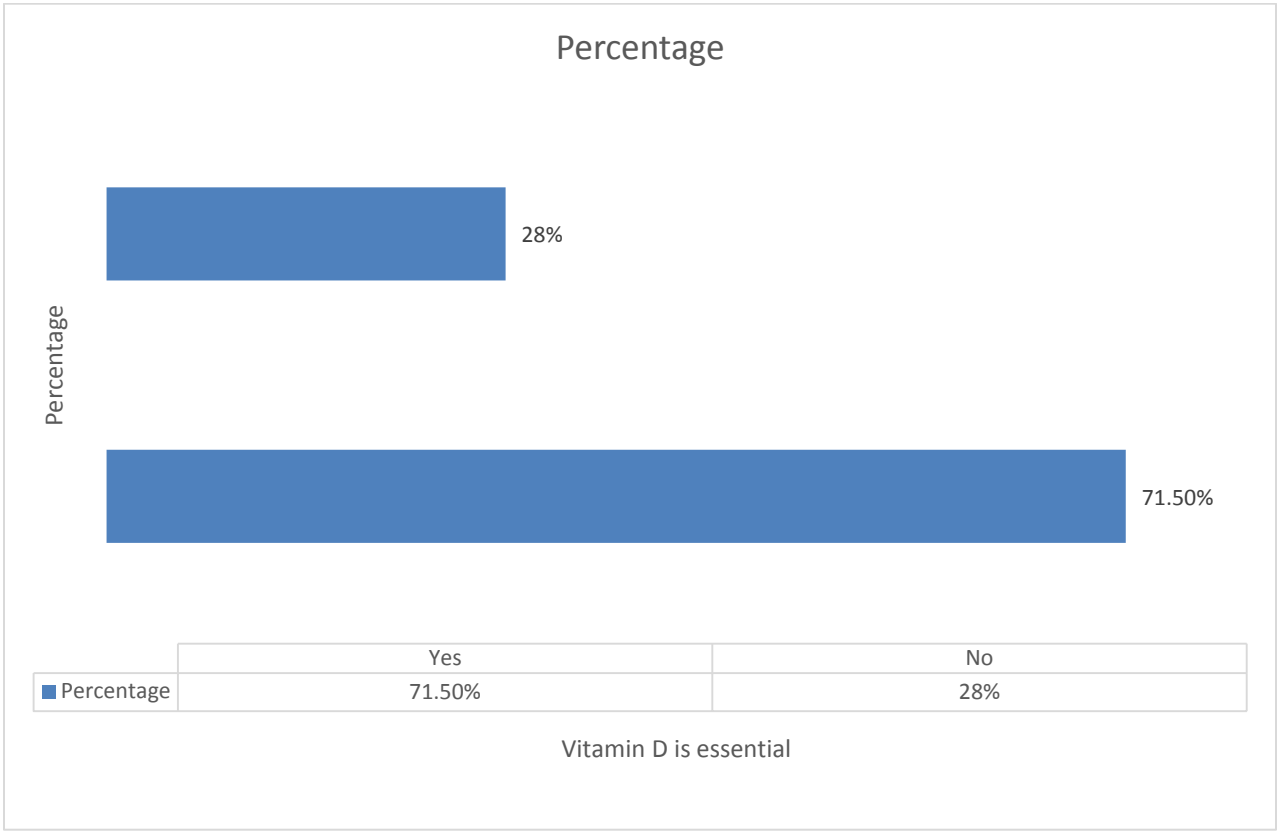



Figure 4.7: Number of respondents who are asked if Vitamin D is essential

Here,we showed that, 71.5% women agree that vitamin D is essential and 28% women don't agree about this.

## 4.8 Number of respondents who are aware of sources of Vitamin D

**Table 4.8 Number of respondents who are aware of sources of Vitamin D**

| Number of respondents who are aware of sources of Vitamin D | Yes | Do not know | Total |
|---|---|---|---|
| Number | 68 | 132 | 200 |
| Percentage | 34% | 66% | |

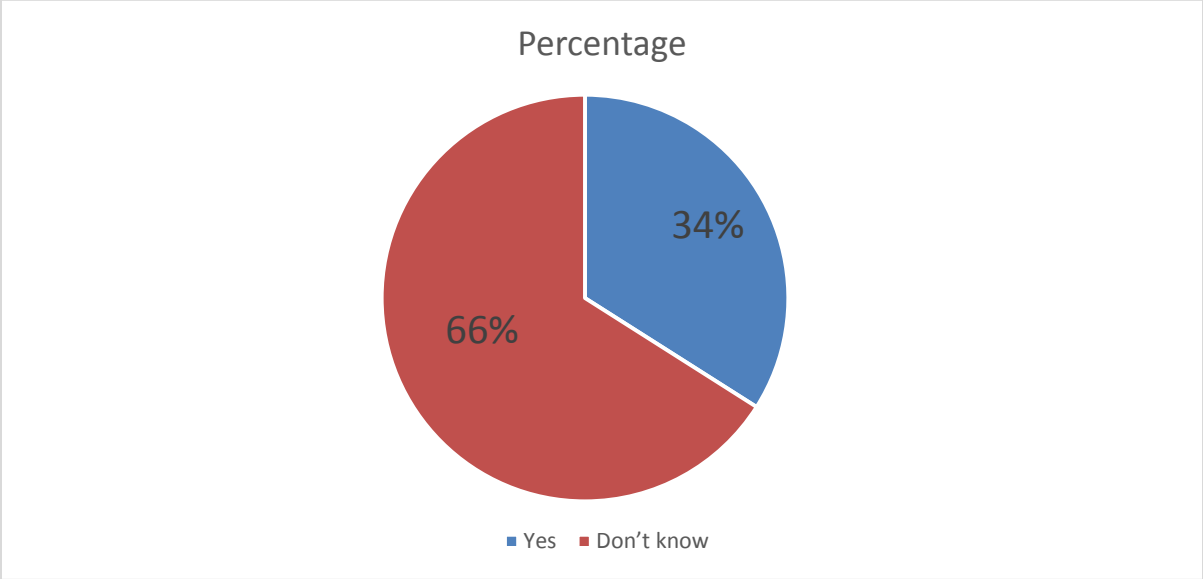



Figure4.8 Number of respondents who are aware of sources of Vitamin D

Here,we found that 66% people don't know about the sources of vitamin D and 34% people know about the sources of vitamin D.

### 4.9 Sources for learning about calcium

**Table 4.9 Sources for learning about calcium**

| Sources for learning about calcium | Percentage | Number | Total |
|---|---|---|---|
| Books | 65% | 130 | 200 |
| Family | 25% | 50 | |
| Internet | 31.50% | 63 | |
| Teacher | 25% | 50 | |
| Media | 25% | 50 | |
| Doctor | 21.50% | 43 | |
| Others | 5% | 10 | |

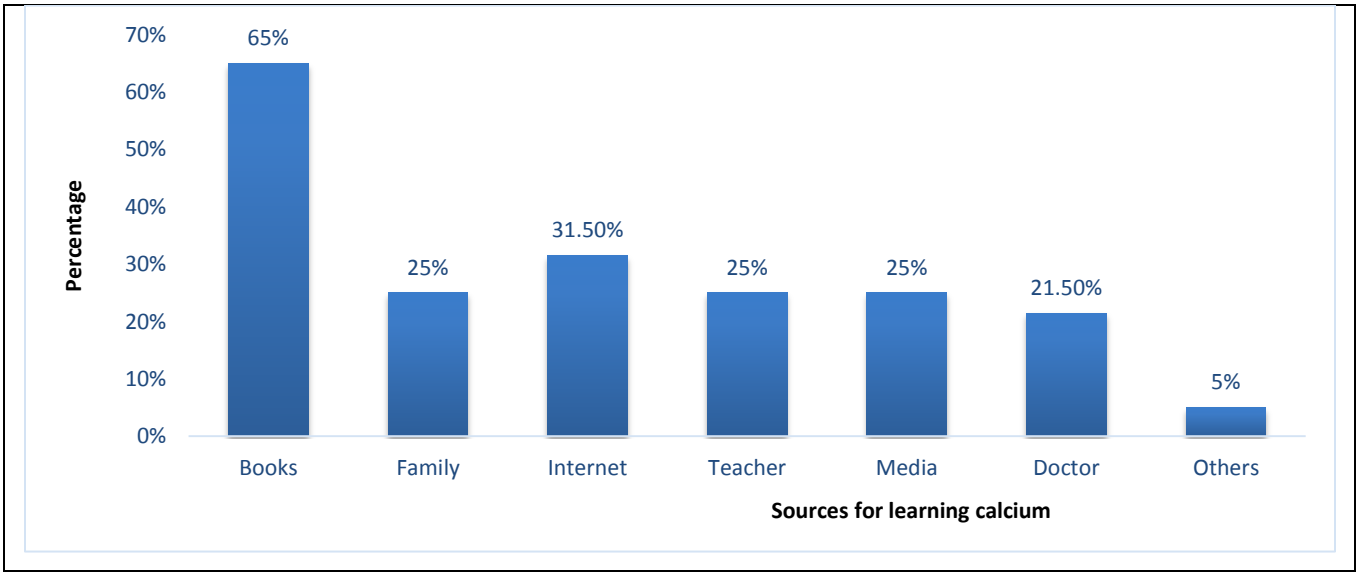



Figure: 4.9 Sources for learning about calcium

Here,we found that 65% people learn about calcium from books,25% learn from family,31.5% from internet,25% from teacher,25% from media,21.5% from doctor,55 from other sources.

### 4.10 Number of respondents who are correctly state about dietary intake of calcium

**Table 4.10 Number of respondents who are correctly state about dietary intake of calcium**

| Number of respondents who are correctly state about dietary intake of calcium | Percentage | Number | Total |
|---|---|---|---|
| Yes | 9.50% | 19 | 200 |
| No | 90% | 180 | |

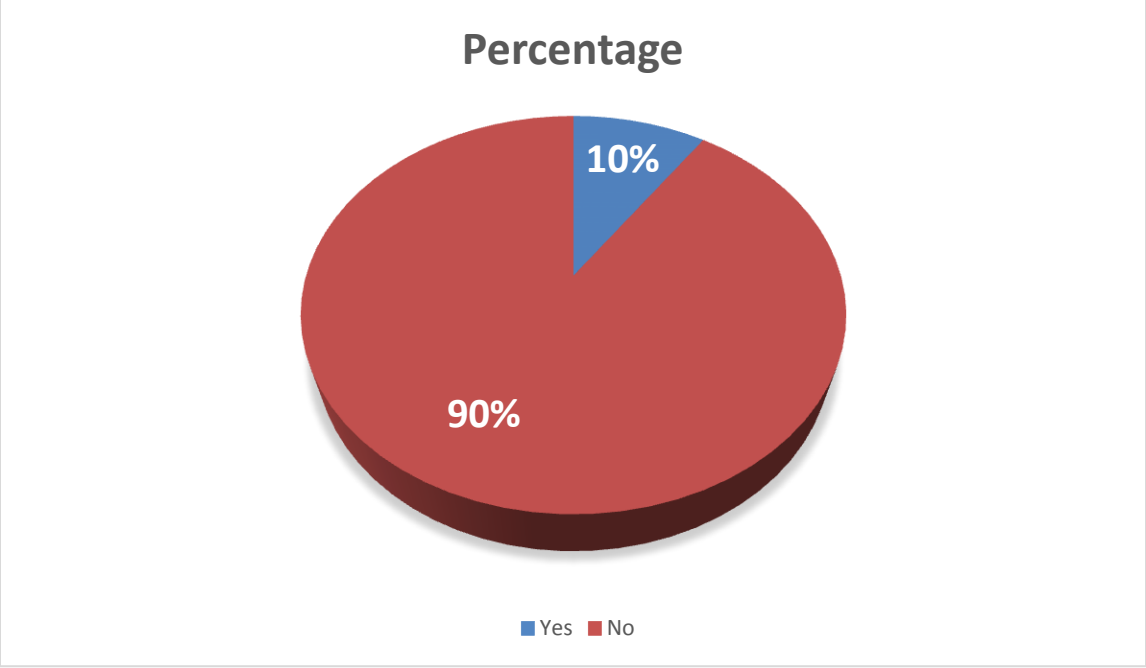



Figure4.10 Number of respondents who are correctly state about dietary intake of calcium

Here,we found that 90% women don't know about the range of daily intake of calcium and 10% know about it.

## 4.11 Number of respondents who are correctly state about dietary intake of calcium

**Table 4.11 Number of respondents who are correctly state about dietary intake of calcium**

| Number of respondents who are correctly state about dietary intake of Vitamin D | Percentage | Number | Total |
|---|---|---|---|
| Yes | 5.50% | 11 | 200 |
| No | 94.50% | 189 | |

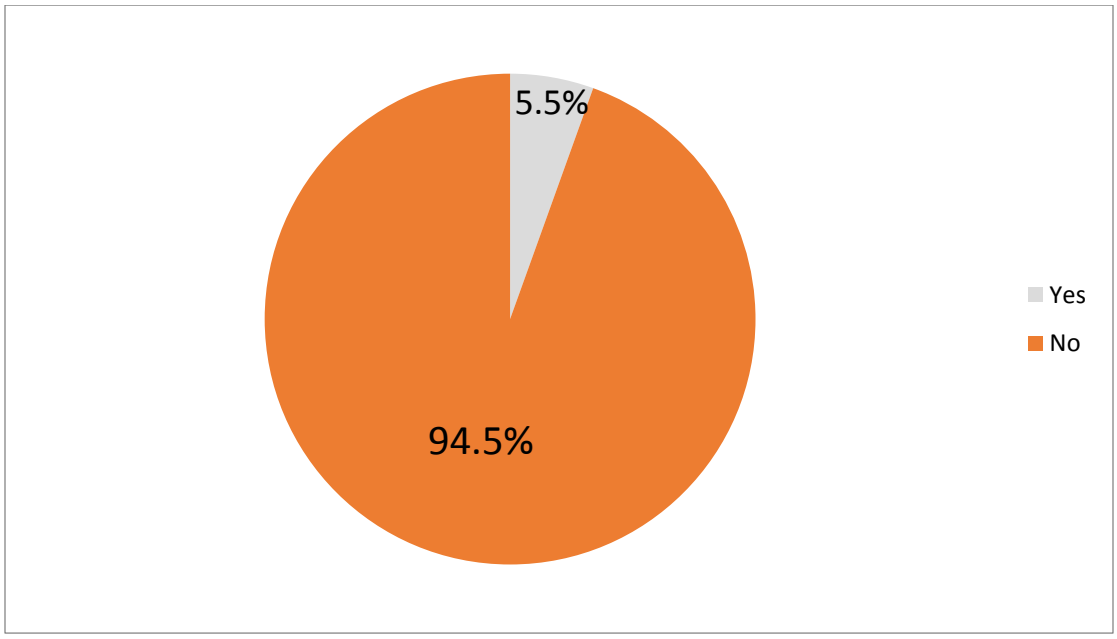



Figure 4.11: Number of respondents who are correctly state about dietary intake of Vitamin D

We showed that 94.5 % responded correctly about dietery intake of Vitamin D.

### 4.12 Number of respondents who knew about calcium

**Table 4.12 Number of respondents who knew about calcium**

| Number of respondents who knew about calcium | Percentage | Number | Total |
|---|---|---|---|
| Yes | 32.50% | 65 | 200 |
| Don't know | 67.50% | 135 | |

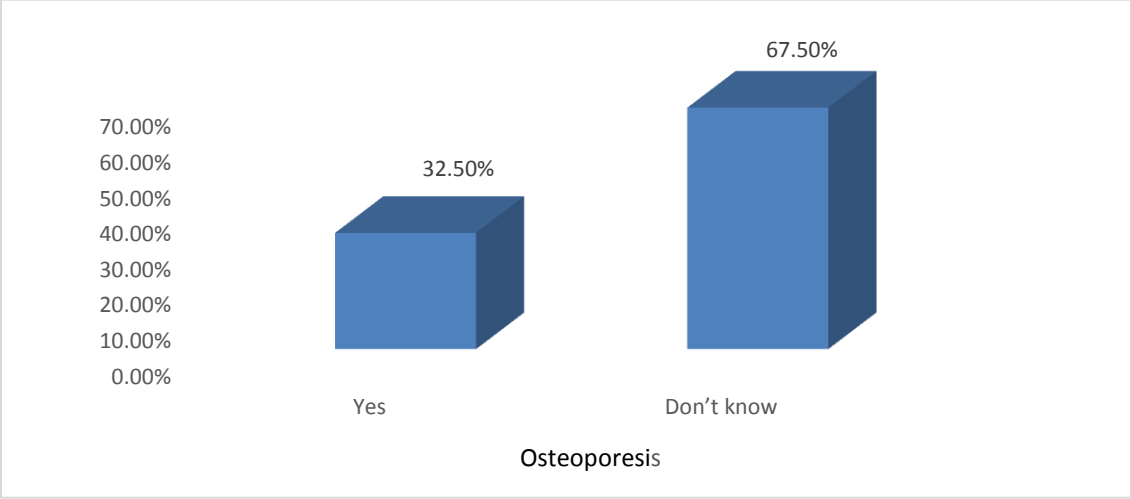



Figure 4.12Number of respondents who knew about calcium

We found in this study that 67.5% women don't know about the disease of osteoporosis and 32.5% know about it.

### 4.13 Number of respondents who are asked if women are more affected than men

**Table 4.13 Number of respondents who are asked if women are more affected than men**

| Number of respondents who are asked if women are more affected than men | Percentage | Number | Total |
|---|---|---|---|
| Yes | 70.50% | 141 | 200 |
| No | 29.50% | 59 | |

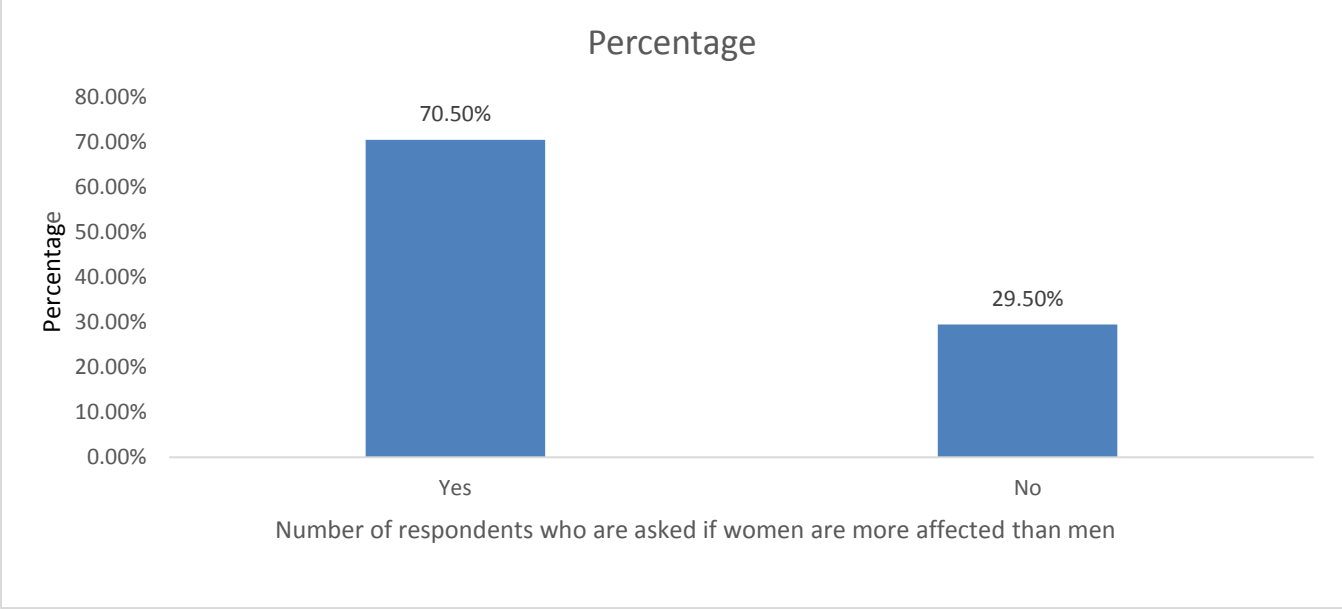



Figure 4.13Number of respondents who are asked if women are more affected than men

Here we found that 70.5% women are agree with us that women are more affected but 29.5% women are not agree with us.

### 4.14 Number of respondents who knew about calcium deficiency diseases of children

**Table 4.14 Number of respondents who knew about calcium deficiency diseases of children**

| Number of respondents who knew about calcium deficiency diseases of children | Response | Number | Total |
|---|---|---|---|
| Yes | 21% | 42 | 200 |
| Don't know | 79% | 158 | |

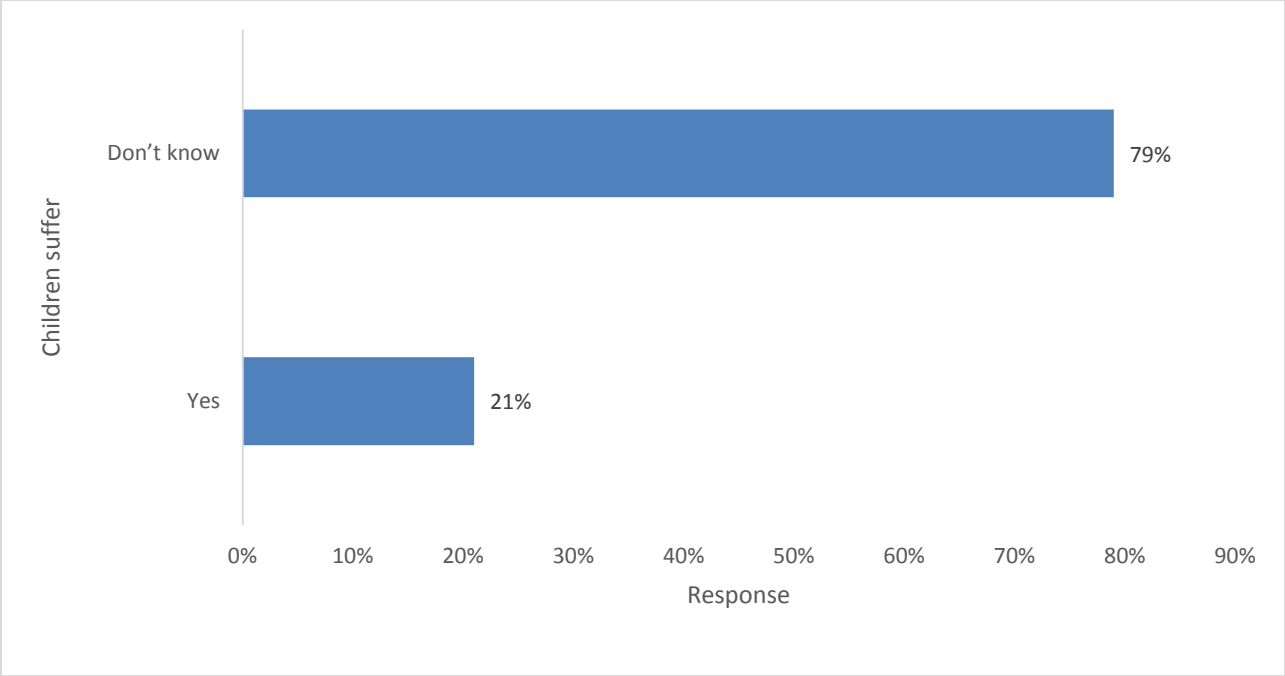



Figure 4.14Number of respondents who knew about calcium deficiency diseases of children

In this study,we found that 79% women don't know about the disease that children suffer due to calcium deficiency and 21% know about it.

### 4.15 Number of respondents who knew about frequency of milk consumption

**Table 4.15 Number of respondents who knew about frequency of milk consumption**

| Number of respondents who knew about frequency of milk consumption | Response | Number | Total |
|---|---|---|---|
| Daily | 68% | 136 | 200 |
| Weekly | 18.50% | 37 | |
| Monthly | 5.50% | 11 | |
| Yearly | 9% | 18 | |
| Never | 10% | 20 | |
| Others | 4% | 8 | |

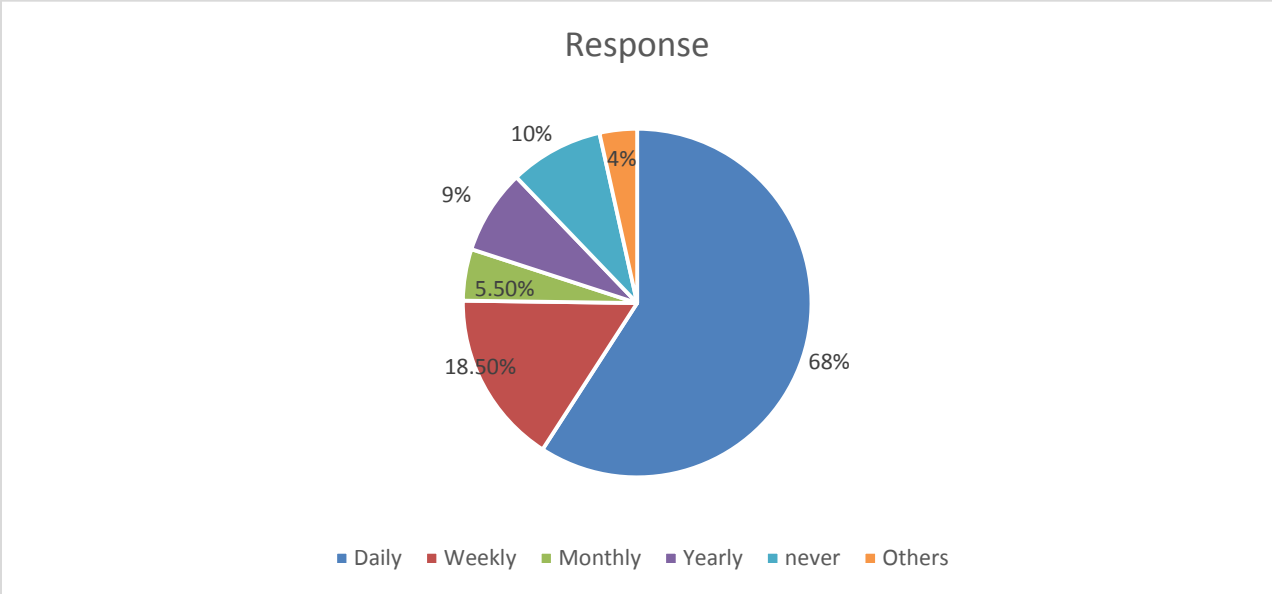


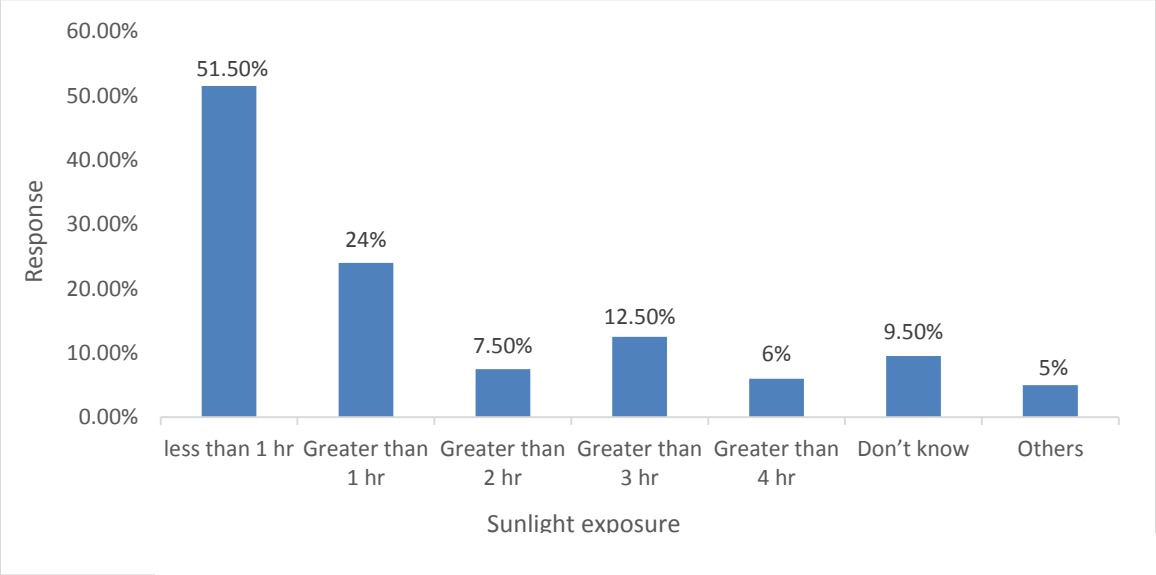

Figure 4.15: Number of respondents who knew about frequency of milk consumption

Among 200 population, daily frequency of child milk consumption is 68%, weekly frequency of child milk consumption is 18.50%, monthly frequency of child milk consumption is 5.50%, yearly frequency of child milk consumption is 9%, daily frequency of child milk consumption is 68%,never consumed milk is 10%, and others is 4%.

### 4.16 Number of respondents who stated about sunlight exposure

**Table 4.15 Number of respondents who stated about sunlight exposure**

| Number of respondents who stated about sunlight exposure | Response | Number | Total |
|---|---|---|---|
| Less than 1 hr | 51.50% | 103 | 200 |
| Greater than 1 hr | 24% | 48 | |
| Greater than 2 hr | 7.50% | 15 | |
| Greater than 3 hr | 12.50% | 25 | |
| Greater than 4 hr | 6% | 12 | |
| Don't know | 9.50% | 19 | |
| Others | 5% | 10 | |




Figure

The study showed that, prevalence of sunlight exposure less than 1 hour is 51.50%, greater than 1 hour is 24%, greater than 2 hour is 7.50%, greater than 3 hour is 12.50%, greater than 4 hour is 6 %, don't know is 9.50%, others 5%.

# Chapter five

## Discussion& Conclusion

## Discussion

In this study some women were asked to mention name of three foods containing calcium and Vitamin D. From the survey it was found that about the 41% &36% women know about it. They were asked if Calcium & Vitamin D is essential as a food supplement while 28% & 22% do not know about the Calcium & Vitamin D. They know about milk (41%), Sea fish (8.5%), Meat (12%), Cheeses (10.5%) and others (27%) as Calcium containing food.

On the basis of drinking milk is response mainly daily (68%).They remain in the high sun exposure per day like >1hr (51.5%). (38%) and (40%) ever been prescribed any Calcium & Vitamin D supplement by a physician while (62%) and (60%) ever not been prescribed.

Women were asked about the source of their knowledge and information they know about calcium and vitamin D. Interestingly most of the women answered that they first knew about calcium and vitamin D from either from textbooks (65%) and their teacher (25%), (31%) from internet, (21.5%) from doctor, (5%) from another sources.

From the responses it was observed that both calcium and vitamin D are equally known among the women. They are not more familiar with the term osteoporosis. The term of “Osteoporosis” are known (22%) of women while (78%) do not know about it.

The women who have science background expected to have adequate knowledge of the essentiality of calcium and vitamin D and the consequences due to lack of calcium and vitamin D. But this study was performed among non science women so from the current study it was observed that most of the women were not familiar with calcium and vitamin D as food supplement. But it seems that they are only familiar to the terminologies, but they do not have sufficient knowledge about the sources from where calcium and vitamin D can be obtained.

The rural women are less familiar with vitamin D ($p<0.001$) and osteoporosis ($p=0.0056$) than urban women, they exercise a healthy diet in terms of milk consumption

($p<0.0001$) and engage themselves more in outdoor activities, spend more time in sunlight ($p<0.0001$) than the urbanwomen. Thus the rural women may require less supplemental support of calcium and/or vitamin D than the urban women.($p<0.0001$).

A study was performed in Vietnam A total of 1,536 individuals aged 14 to 85 years participated in the study. Fifty three percent of participants did not like being exposed to sunlight. On the average, most reported approximately 14 hours per week under the sun. Majority (81%) reported that they had heard of vitamin D from newspapers (32%), friends (20%) or radio and television (13%). However, their knowledge about the source of vitamin D was inadequate: 37% thought that vitamin D comes from the sun, 28% from foodstuff and the sun, while 17% did not know the source of vitamin D. Analysis of the determinants of knowledge of vitamin D suggested that only educational level was a significant predictor of vitamin D knowledge.

One interesting finding of my study is that, most of the women first heard about calcium and/vitamin D from academic sources (from their teachers and textbooks). In Bangladesh women know about Calcium & Vitamin D only from doctor or from their family sometimes from books. But illiterate women were not aware of Calcium and Vitamin D. Vitamin D and calcium deficiency is so common as to represent a major public health problem. It has re-emerged as a global public-health concern and is now linked to a range of infectious, inflammatory and neoplastic diseases throughout the life course and around the world. Country specific sufficient data regarding the use, consumption of calcium and vitamin D for Bangladesh is not available though some studies have been conducted for the determination of vitamin D and calcium status.

## Conclusion

Calcium and Vitamin D are the important component of a healthy diet and a mineral necessary for life. The National foundation says, “Calcium plays an important role in building stronger, denser bones early in life and keeping bones strong and healthy later in life”. Approximately 99% of body’s calcium is stored in the bones & teeth. The rest of the calcium in the body has other important uses, such as some exocytose. The effects of vitamin D supplementation on health are uncertain. A United States Institute of Medicine, (IOM) report states: "Outcomes related to cancer, cardiovascular disease and hypertension, diabetes and metabolic syndrome falls and physical performance, immune functioning & autoimmune disorders, infections, neuropsychological functioning, and preeclampsia could not be linked reliably with calcium or vitamin D intake and were often conflicting. So the questions regards to safety and efficacy awareness of calcium and vitamin D among women and children in Bangladesh.

From this survey, we have come to know that the womenwho are non science background do not have adequate knowledge of essential nutrients, minerals, vitamins etc. If they have gap of knowledge about calcium and vitamin D, their children may know little about these food supplements. The government and policy makers should pay attention about improving this situation by utilizing mass media and print media to increase awareness regarding calcium and vitamin D.

# Chapter six
# Reference

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