

# Vitamin D deficiency in Children: An update

Abdulmoein Eid Al-Agha, MBBS, DCH, FRCPCH

Professor of Pediatric Endocrinology, King  
Abdulaziz University Hospital

, Jeddah, Saudi Arabia

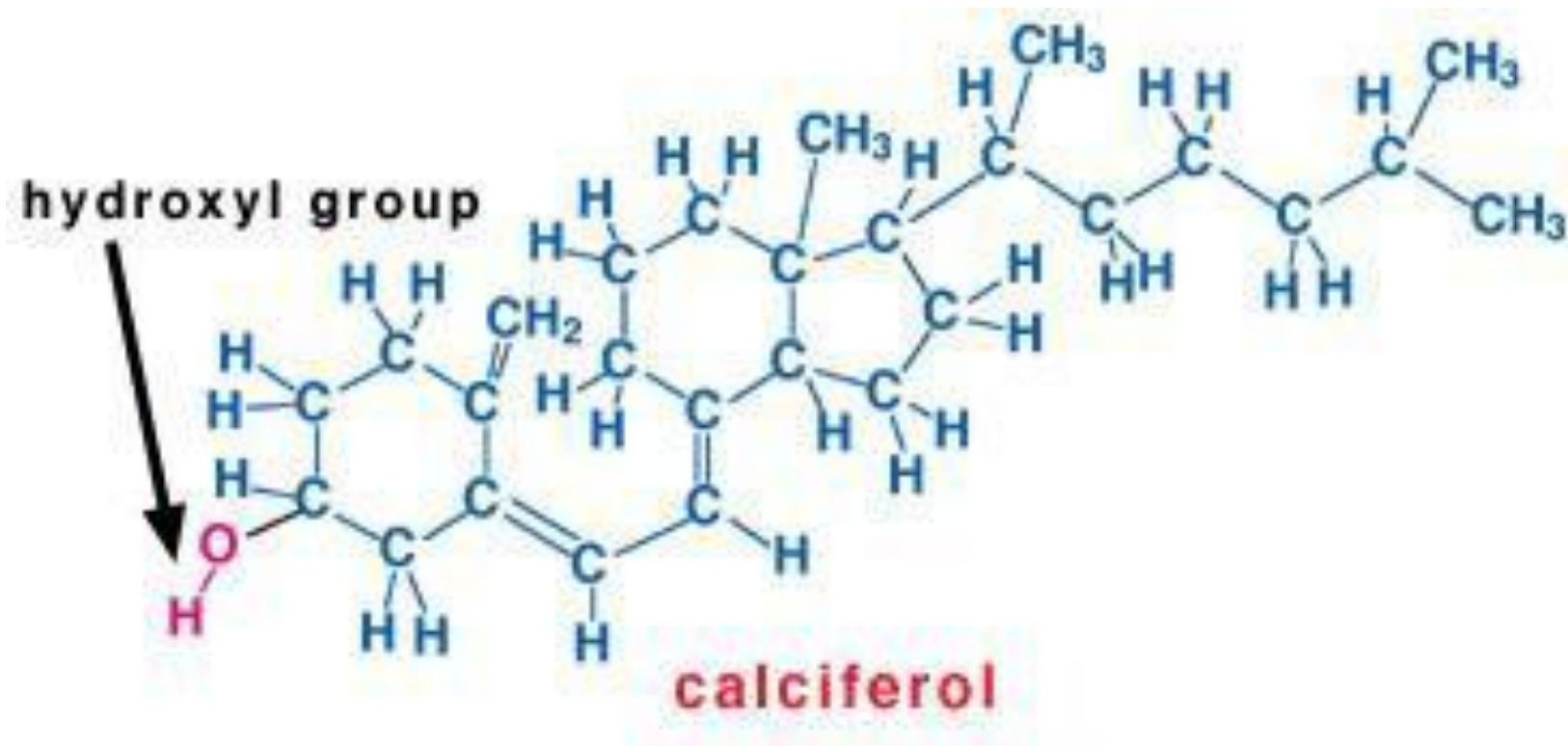
Website: <http://aagha.kau.edu.sa>

# Outline

- Introduction.
- Vitamin D metabolism.
- Vitamin D resources.
- Vitamin D Benefits.
  - Both on skeletal & 'extra-skeletal' benefits of vitamin D.
- Vitamin D Deficiency
  - Definition.
  - Causes.
  - Symptoms & signs.
  - Laboratory findings.
  - Radiological findings.
- Prevention & Treatment.

# Vitamin D 'Calciferol'

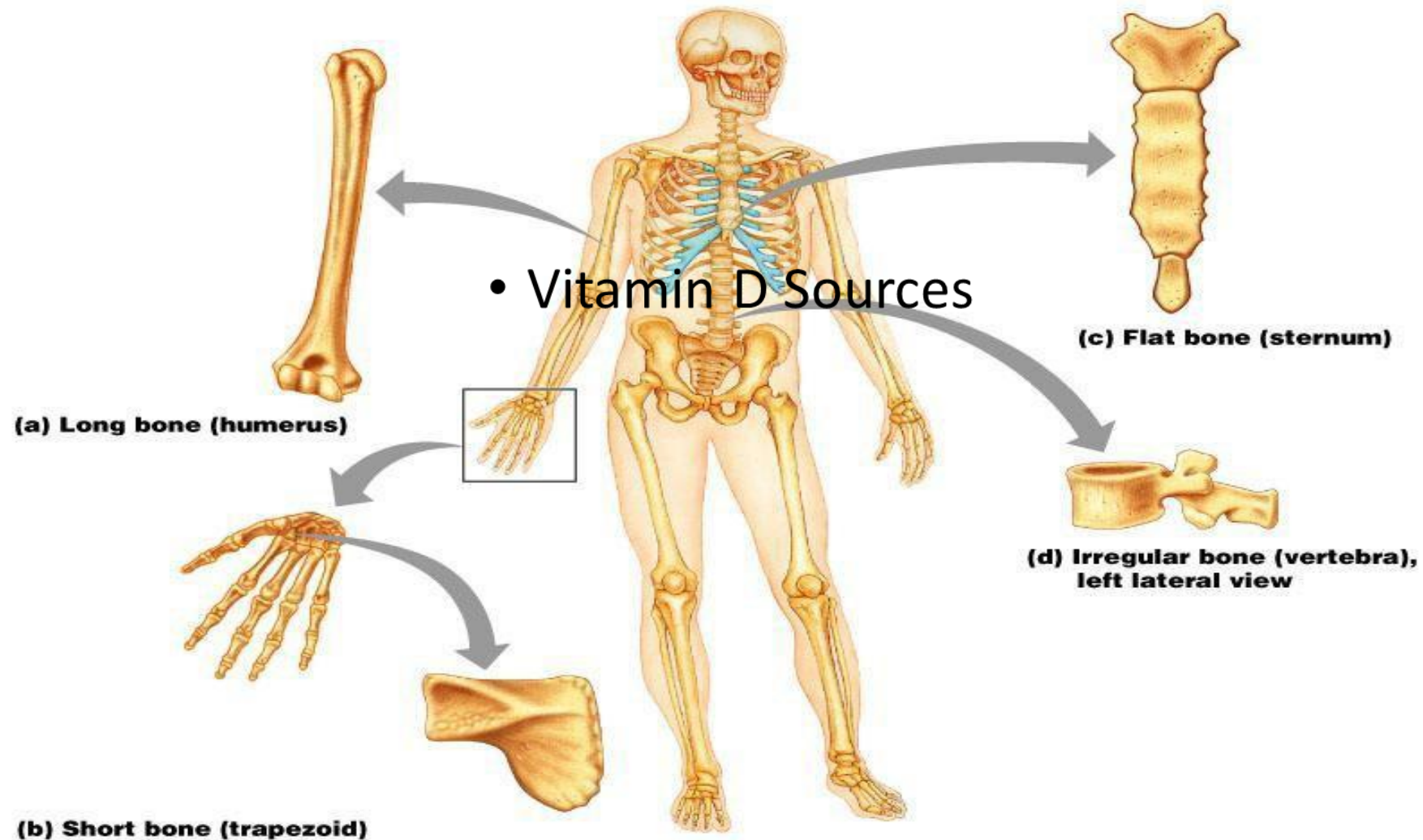
- Lipid-soluble vitamin & Hormone with a 4-ring cholesterol backbone



# Introduction

- Vitamin D is an extremely important vitamin that has powerful effects on several systems of the body.
- Unlike other vitamins, vitamin D functions like a hormone & every single cell in the body has a receptor for it.
- Vitamin D deficiency is very common medical condition in Saudi Arabia.
- It's estimated that about 1 billion people worldwide have low levels of
  - the vitamin D.
    - All age groups are affected!
    - 41.6% of adults in the US are deficient.
    - 69.2% in Hispanics and 82.1% in African-Americans .
    - 90 -95 % prevalence in Saudi Arabia.

# Primary role is bone mineralization with secondary role on bone density



# Skeleton is solid but still a dynamic tissue !

- Skeleton is not static structure, but in continuous process of "modeling - remodeling"
- Bone is continually remodeled throughout life span because of sustain recurring micro-trauma
- The hallmark of Rickets/ Osteomalacia is decreased bone mineralization (calcium/phosphate or both)
- The hallmark of osteoporosis is reduction in skeletal mass caused by imbalance between bone resorption & bone formation

# Vitamin D Resources

- Both **Ergocalciferol (D2)** & **cholecalciferol (D3)** are equipotent, both increase vitamin D stores to varying degrees, however, recent evidence suggests that vitamin D3 increases vitamin D concentrations two - to threefold more than D2.
- Despite the evidence suggesting the pharmacodynamic differences between D3 and D2, **most guidelines do not have a preference between the 2 products.**
- Vitamin D is available commercially as ergo-calciferol, cholecalciferol, one alpha Calcidiol & calcitriol.

# Vitamin D Resources

- Nearly 90% of Vitamin D requirement (Vitamin D3) is met by adequate exposure of the skin to sunlight through the action of Ultraviolet B Radiations (UVR) and remaining 10% is said to meet through diet.
- The commonest dietary resources of Vitamin D3 are animal food sources e.g., fish (e.g., salmon and tuna), cod liver oil, milk and all fortified milk products, whereas Vitamin D2 is found in plant sources like yeast and mushrooms.
- The WHO expert consultation states that humans can get vitamin D from abundant sunshine, by exposing 18% of body surface area (without sunscreen) to mid-day sun (10 am-3 pm) for average of 15-30 min/day (depends on skin color (white/ fair or dark pigmented skin)).



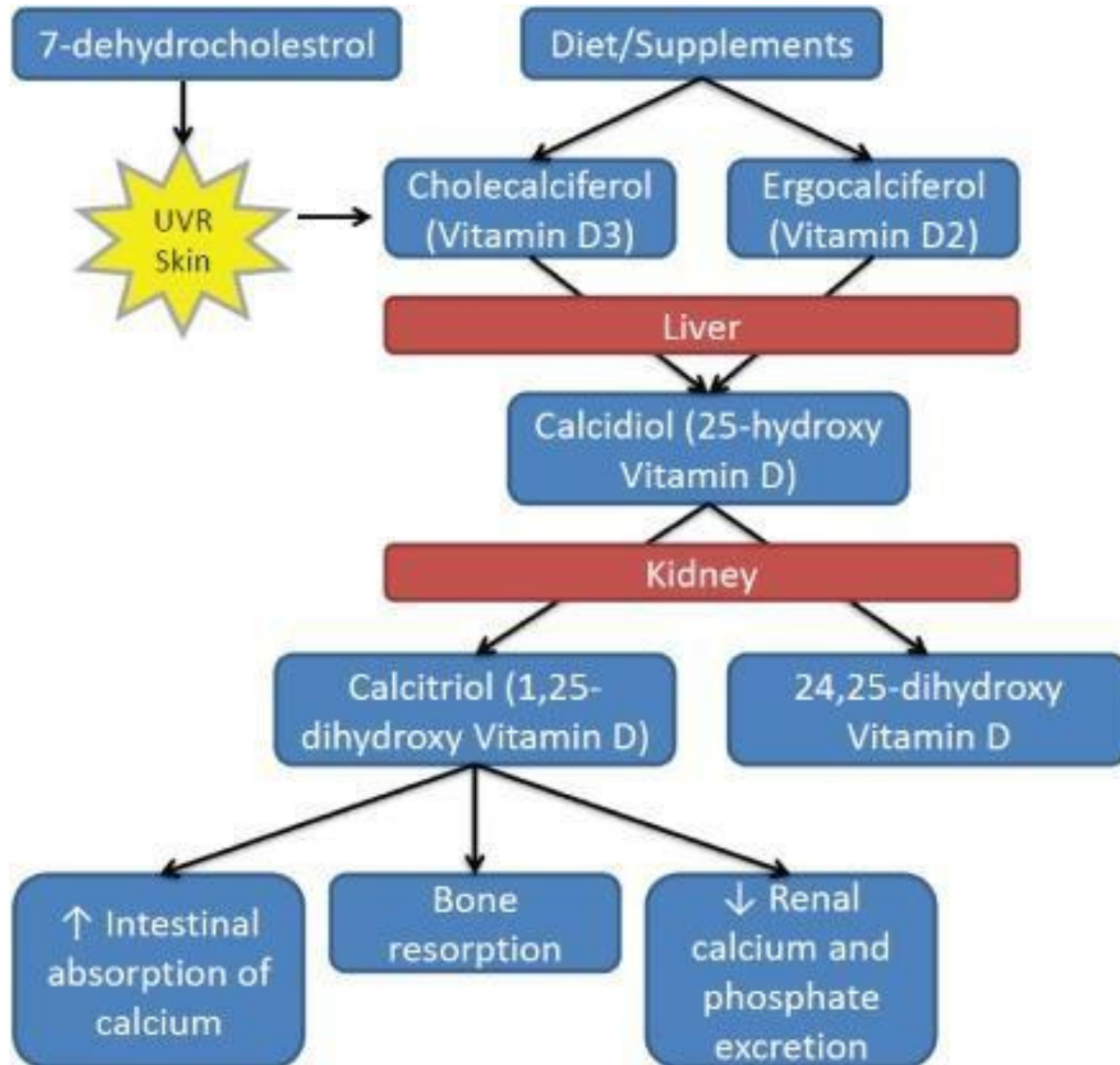
Sun is the most powerful source of  
vitamin D



# Vitamin D in Breast Milk

- Breast milk contains little amount of vitamin D, an average of 22 units/L (range 15 to 50 units/L) in a vitamin D-sufficient mother .
- Recent studies suggest that **maternal intake of vitamin D (4000 to 6000 units daily)** may achieve vitamin D concentrations in breast milk to provide sufficient vitamin D supplementation for breastfeeding infants.
- The recommendation for exclusively breastfed infants is to provide them with **a supplement of 400 units per day** (increased from previous recommendations of 200 units per day).

# Vitamin D Metabolism



# Vitamin D metabolism

- Both forms of Vitamin D are metabolized in the liver to produce initially; 25(OH)D (Calcidiol) followed by 1,25,(OH)<sub>2</sub> Vitamin D (Calcitriol) in the kidney.
- The majority of the circulating 25(OH)D is tightly bound to **vitamin D Binding Protein (DBP)**, which is an albumin-like protein synthesized in the liver.
- DBP-bound 25OHD pathway in the proximal tubule epithelium allows for hydroxylation of 25OHD by 1- $\alpha$  hydroxylase to produce **1,25(OH)<sub>2</sub>D, the active metabolite of vitamin D** for systemic/endocrine functions .

# Vitamin D Benefits

# Vitamin D Benefits on Skeleton

- Vitamin D is very important for humans skeleton as well, non skeleton tissues right from conception throughout lifespan.
- Since approximately 40%-60% of total skeletal mass at maturity is accumulated during childhood & adolescence, it has major implications on adult bone health.
- Additionally, is important for children , of its profound effect on growth & development.
- It regulates calcium & phosphorus balance for bone mineralization & bone remodeling.

Vitamin D3 not only for strong bones!!

# Extra - skeletal benefits of vitamin D

- Vitamin D is believed to act as a potent antioxidant protecting against free radical damage and an inducer of cellular differentiation, protecting against carcinogenesis.
- It also has a role to fight against serious infections, by controlling T Cell antigen receptor (TCR) signaling and activation of human T cells.
- Vitamin D deficiency, could therefore, be associated with an increase in risk for certain diseases.
- Since these diseases are multifactorial, optimum vitamin D levels may not
  - prevent these diseases, but their risk is lowered.
- In pediatric age group, subclinical vitamin D deficiency & nonexclusive breastfeeding in the first 6 months of life were found to be significant increase risks for acute respiratory tract infections , tuberculosis as well other diseases.
- Significant inverse relationship between Vitamin D levels and severity of Asthma, COPD were observed in some studies.



# Role of vitamin D in Cancer Prevention

- Low intake of vitamin D and calcium has been associated with an increased risk of non-Hodgkin lymphomas, colon, ovarian, breast, prostate, and other cancers.
- The anti-cancer activity of vitamin D
  - a nuclear transcription factor that regulates cell growth, differentiation, & apoptosis, central to the development of cancer.

# Role of vitamin D in reducing risk of Autoimmune Disease

- Vitamin D supplementation is associated with a lower risk of autoimmune diseases.
- In a Finnish birth cohort study of 10,821 children, supplementation with vitamin D at 2000 IU/d reduced the risk of type 1 diabetes by approximately 78%, whereas children who were at risk for rickets had a 3-fold higher risk for type 1 diabetes.
- In a case-control study of 7 million US military personnel, high circulating levels of vitamin D were associated with a lower risk of multiple sclerosis.
- Similar associations have also been described for vitamin D levels and rheumatoid arthritis.

## Role of vitamin D in reducing risk of Cardiovascular Diseases

- Vitamin D deficiency activates the renin-angiotensin-Aldosterone system and can predispose to hypertension and left ventricular hypertrophy.
- Additionally, vitamin D deficiency causes an increase in parathyroid hormone, which increases insulin resistance secondary to down regulation of insulin receptors and is associated with diabetes, hypertension, inflammation, and increased cardiovascular risk.

## Role of vitamin D in Reproductive Health

- Vitamin D deficiency early in pregnancy is associated with a five-fold increased risk of preeclampsia.
- Researchers concluded that having low levels of vitamin D (<17.8 ng/mL) was independently associated with an increase in all-cause mortality in the general population.

## Role of vitamin D in management of dermatology

- Topical Vitamin D (Calcipotrol) has been proven to be effective in management of Psoriasis.
- Studies have also depicted association of Vitamin D intake and reduced risk of T1DM and 30% reduction in risk.

Some of my own publications on  
beneficial effects of vitamin D

## Association among Vitamin D Deficiency, Type 1 Diabetes Mellitus and Glycemic Control

Abdulmoein E Al-Agha<sup>1,2\*</sup> and Ihab A Ahmad<sup>3</sup>

<sup>1</sup>Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

<sup>2</sup>Department of Pediatrics, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

<sup>3</sup>Department of Pediatrics, Faculty of Medicine, Zagazig University, Zagazig, Egypt

### Abstract

**Background:** Studies have identified that the deficiency of vitamin D is strongly connected with diabetes mellitus type 1. Vitamin D has the capability to control increased blood glucose level.

**Purpose:** The study appraises the association among vitamin D deficiency, type 1 diabetes mellitus, and glycated hemoglobin among children.

**Methods:** Around, 226 diabetic children were selected for this retrospective study from outpatient department of King Abdul Aziz University Hospital. Majority of the participants were female individuals, with the rate of 61.1% and were divided into three categories, based upon the rate of vitamin D deficiency. Every participant of the study was taking intensive insulin therapy.

**Results:** The findings of the study have shown that 77% of the diabetic patients had reduced level of vitamin D in total. The study identified, from the evaluation between HbA1c control and vitamin D status, that 66% of the diabetic and vitamin D deficient participants were poorly controlled (HbA1c>9%).

**Conclusion:** Vitamin D deficiency among the patients of diabetes mellitus type 1 was extremely high and was closely related with glycemic control. Additionally, the findings of the study have demonstrated therapeutic implications that the supplements of vitamin D have the potential to manage glucose level.



## **Association between vitamin D deficiency and weight gain in children: A cross-sectional study.**

**Randa A Sultan, Raghda A Sultan, Abdulmoein Eid Al-Agha\*, Areej O Mahjoub**

Faculty of Medicine, Department of Pediatrics, King Abdulaziz University, Jeddah, Saudi Arabia.

### **Abstract**

**Introduction:** Obesity in children is a serious and growing health problem. Its prevalence has significantly increased over the past decades. Obesity is a risk factor for increased morbidity and mortality and is a multifactorial condition. Recently, studies on the association between vitamin D deficiency and obesity have been conducted. This study aimed to determine the relationship between vitamin D deficiency and weight gain in children in Jeddah, Saudi Arabia.

**Methods:** This cross-sectional study included 321 healthy children (176 girls and 145 boys) from an ambulatory pediatric clinic at King Abdul-Aziz University Hospital between November 2017 and April 2018. The anthropometric variables of each child were obtained, and blood samples were obtained to measure vitamin D, thyroid and parathyroid hormone, and calcium levels.

**Results:** The participants included 176 (54.8%) girls and 145 (45.2%) boys with a mean age of  $9.8 \pm 3.8$  yrs. The average body mass index was  $18.01 \pm 3.5$  kg/m<sup>2</sup>, and the mean vitamin D level was  $26.4 \pm 10.6$  nmol/L for both sexes. Vitamin D deficiency was identified in 96.5% of the participants, and only 3.5% had normal vitamin D levels. A significant association was observed between body weight and vitamin D deficiency (P value=0.013 and Pearson correlation coefficient=-0.2). The results showed an inverse relationship between vitamin D deficiency and body weight, i.e., any decrease in vitamin D levels inversely affected body weight.

**Conclusion:** Vitamin D deficiency was inversely associated with weight gain in children.

# The Benefit of Vitamin D Therapy on Psychological Aspects in Children and Adolescents in Western Saudi Arabia

Lama Khaled Arfaj, Suzan Abu Alainain and Abdulmoein Eid Al-Agha\*

*Pediatric Department, King Abdulaziz University Hospital, Jeddah 21589, Saudi Arabia*

\*Corresponding author: Abdulmoein Eid Al-Agha, Professor of Pediatric Endocrinology, King Abdulaziz University Hospital, Jeddah 21589, Saudi Arabia, Tel: 00966505590459; Fax: +96626403841, E-mail: [aagha@kau.edu.sa](mailto:aagha@kau.edu.sa)

Received date: June 03, 2017; Accepted date: June 26, 2017; Published date: June 30, 2017

Copyright: © 2017 Arfaj LK, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract

**Background:** Vitamin D deficiency is a major public health problem worldwide, including in children of Saudi Arabia. Vitamin D has numerous beneficial skeletal and non-skeletal physiological effects. Vitamin D is not only essential for bone health, but also promotes proper brain development and functioning. Vitamin D also serves many important functions, such as promoting calcium absorption and reducing inflammation.

**Aim:** To investigate the relationship between vitamin D deficiency and psychological impacts in children and adolescents, and to determine whether vitamin D therapy has beneficial psychological effects in this population.

**Study design:** This cross-sectional study was conducted in Jeddah, Saudi Arabia. The sample included 181 young children and adolescents between 2 and 18 years of age (88 females, 93 male) from various regions of the city. Relevant data were collected during clinic interviews. Data were analyzed using a chi-square test for nominal data. Interview data were used to compare pre- and post-vitamin D treatment factors.

**Results:** Psychological manifestations associated with vitamin D deficiency were commonly seen between 6-12 years of age (40.9%), 2-6 years of age (38.1%), and 12-18 years of age (21.0%). Males (51.4%) exhibited higher rate of deficiency when compared to females (48.6%), although this relationship was not statistically significant ( $p$ -value=0.441). Most males and females displayed insufficient vitamin D levels. A significant improvement in psychological symptoms was noted with vitamin D therapy ( $p$ -value<0.05).

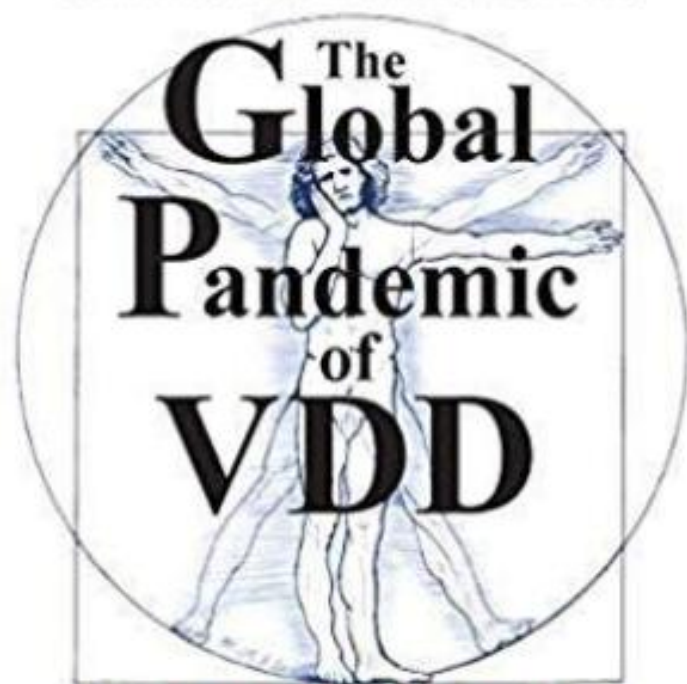
**Conclusion:** A correlational relationship between vitamin D deficiency and psychological problems was revealed in children and adolescents, through comparison of improvements psychological issues following vitamin D therapy.



# Vitamin D deficiency

CHANGE YOUR HEALTH — CHANGE YOUR LIFE

Discover Over 300 Ways  
**Vitamin D Deficiency**  
Can Affect Your Health & Your Life



**KING OF ALL SILENT KILLERS**

*Immediate actions are urgently needed to protect the  
global population from Vitamin D Deficiency.*

*Journal of Preventive Medicine & Public Health — 2017*

David C. Page, D.D.S.

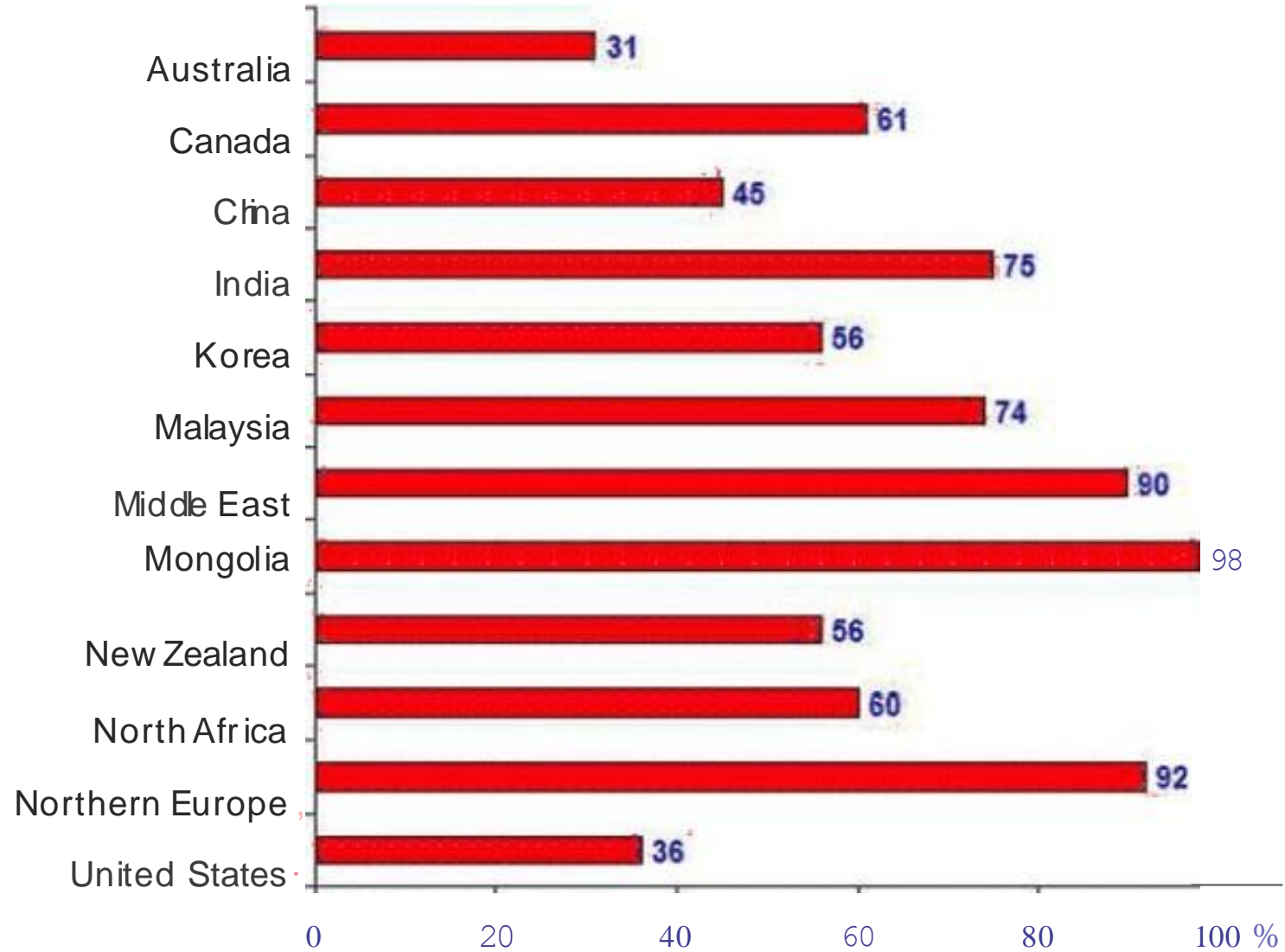
**Vitamin D**  
deficiency is a major common health issue worldwide  
**in all age groups**



# When to say vitamin D is deficient??

- Vitamin D deficiency is typically diagnosed by measuring the concentration of the serum level of 25- hydroxy vitamin D, which is the most accurate measure of stores of vitamin D in the body.
  - Deficiency: < 20 ng/mL
  - Insufficient: 20–29 ng/mL
  - Normal: 30–100 ng/mL
- Vitamin D levels falling within this normal range prevent clinical manifestations of vitamin D insufficiency / deficiency
  - Multiply ng/ml by 2.5 to get nmol/l

## Many countries have large % of population with less than 20 ng of vitamin D



# Prevalence & attributing factors

- It is observed that inadequate sun exposure contributes significantly to Vitamin D deficiency in children.
- Pollution results in high haze score which hinders solar UVB rays reaching the ground because of high haze score.
- The lack of space, overcrowded tenements prevent the direct sunlight reaching inside most parts in urban regions and gives limited scope for outdoor activities among children.
- The extreme discomfort of **the hot weather** keeps children away from the midday sun exposure between 10 am to 3 pm making population susceptible for Vitamin D deficiency owing to inadequate sun exposure.
  - High phytate (Chapati bread and/ or low calcium diet are likely mechanisms for Vitamin D deficiency among children despite adequate sun exposure.

# Rickets/ Osteomalacia

- Rickets is a disease of the **growing bones** in which defective mineralization occurs in both bone & cartilage of the epiphyseal growth plates.
- It is associated with growth retardation & skeletal deformities
  - Skeletal muscles have a vitamin D receptor
  - Vitamin D deficiency causes muscle weakness
- Osteomalacia is a disorder of the **mature bone** in which mineralization of new osteoid bone is inadequate or delayed.

# Causes of vitamin D deficiency

- Lack of vitamin D due to:
  - Decreased sun exposure (hot weather , dark skin)
  - Dietary-deficient intake of fortified milk products, fish.
  - Malabsorption diseases that affects absorption of vitamin D (e.g. celiac disease, CF, chronic diarrhea...etc)
- Chronic liver diseases (affects conversion of cholecalciferol to Calcidiol).
- Anticonvulsant medications (phenytoin, phenobarbitone due to increased metabolism of vitamin D by inducing cytochrome P450 activity).

- Malabsorption diseases.
  - Celiac disease.
  - Pancreatic insufficiency.
    - Cystic fibrosis.
    - Chronic diarrhea.
- Hepato-biliary disease.
  - Biliary Arteresia.
  - Cirrhosis.
  - Neonatal hepatitis.
- Chronic renal failure (Renal Osteodystrophy).
- RTA (Renal Tubular Acidosis).



# Symptoms & Signs of vitamin D deficiency

# Symptoms & Signs of vitamin D deficiency

- It could be Asymptomatic!
- Bowing of the legs/ knock knees especially in children
  - Rickets / Osteomalacia.
- Excessive fatigue & tiredness (common symptoms in both adults & children).
- Bone pains (back pain is the commonest, legs and other bones), sometimes severe enough to prevent daily activities.
- Muscle spasms, twitchiness, weakness & cramps.
  - There is a link between chronic pain and low levels of vitamin D, which may be due to the interaction between the vitamin D & pain-sensing nerve cells.
- Depression is associated with low vitamin D levels and some studies have found that vitamin D supplementation improves mood.
- Hair loss (especially in females) leading to alopecia areata.

# Clinical Presentations of Vitamin D Deficiency in Children at King Abdul-Aziz University Hospital, Jeddah, Saudi Arabia: A Cross-Sectional Survey

Abdulmoein Aagha E<sup>1\*</sup>, Raneem Abushanab H<sup>2</sup>, Huda Balt o M<sup>2</sup> and Duaa Alahdal M<sup>2</sup>

<sup>1</sup>Department of Paediatrics, King Abdul-Aziz University Hospital, Jeddah, Saudi Arabia

<sup>2</sup>King Abdul-Aziz University Hospital, Saudi Arabia

corresponding author: Abdulmoein Aagha E, Department of Paediatrics, King Abdul-Aziz University Hospital, Jeddah 22252, Saudi Arabia, Tel: 0505590459; Fax: +966-2-6408306; E-mail: [aagha@kau.edu.sa](mailto:aagha@kau.edu.sa)

Received date: Jan 1, 2016; Accepted date: June 10, 2016; Published date: June 17, 2016

Copyright: © 2016 Aagha AE, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract

**Objectives:** This study assessed clinical presentations of vitamin D deficiency in Saudi Arabian children.

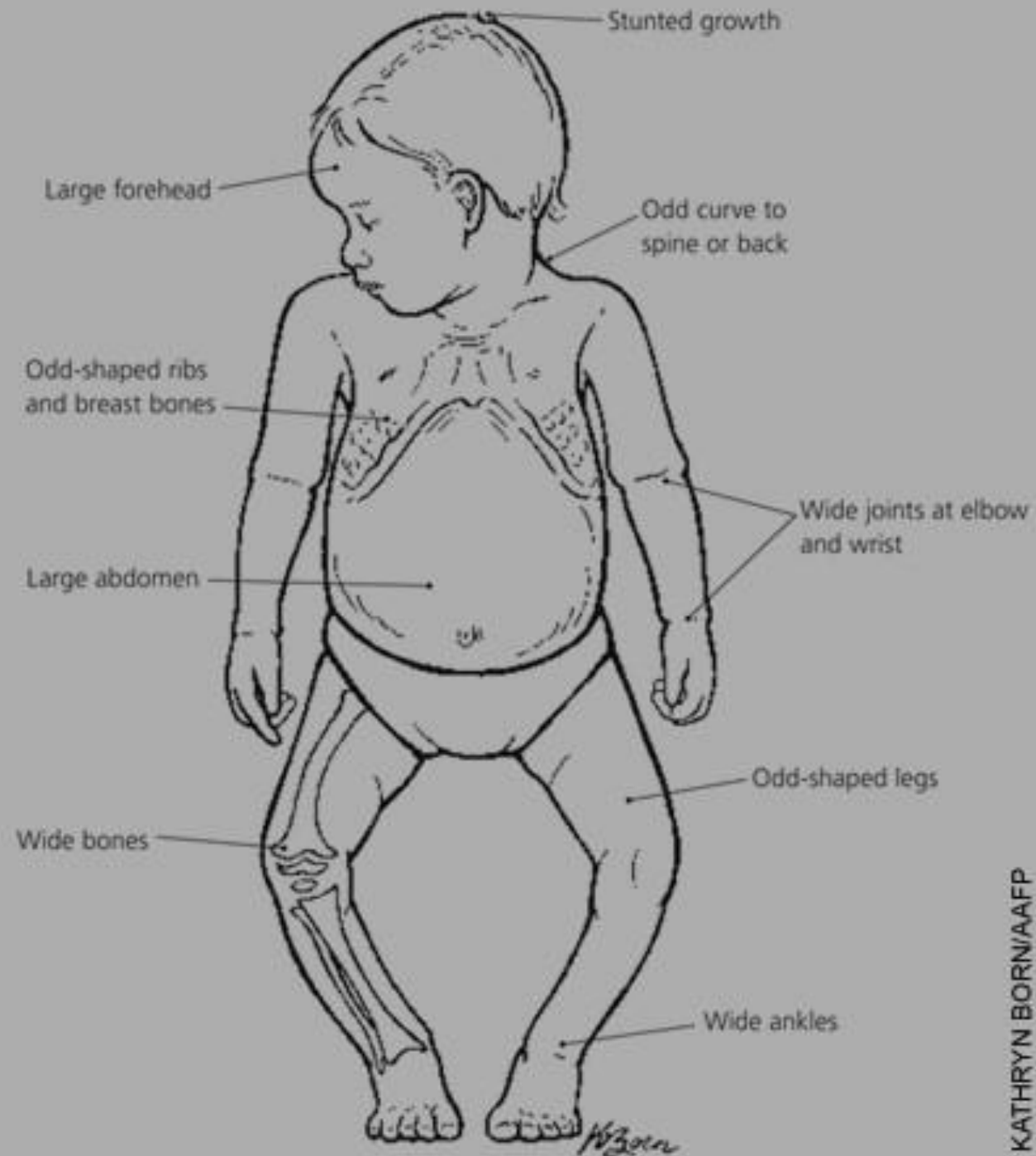
**Methods:** This cross-sectional survey was conducted in the Paediatric Clinic at King Abdul-Aziz University Hospital in Jeddah from March to September 2015. This study included 371 healthy children, not known to have any medical illnesses between the ages of 2 and 18 years old discovered to have vitamin D deficiency. The families of the children were asked if they noticed any symptoms of vitamin D deficiency in their children. A diagnosis of vitamin D deficiency was made if blood tests found low levels of 25-hydroxyvitamin D, there is no other test done to them.

**Results:** Of the population studied, 35 children had a past history of bone fractures, 70 had bone or joint pain, 55 had fatigue, 16 had depression, 28 experienced delayed teething, 7 had a bone deformity, 23 experienced delayed walking, 11 had delayed closure of fontanelles, 5 had developmental delays, 4 exhibited rachitic rosary, 8 had bowing of the legs, 2 had kyphosis, and 71 children were asymptomatic.

**Conclusion:** Joint pain was the most common presentation of the disorder followed by asymptomatic vitamin D deficiency in this population. So, routine screening for preschool children and adolescent is necessary to early detect and provide effective treatment.

**Keywords** Vitamin D; Children; Deficiency; Presentation

Life-threatening hypocalcemia may present with convulsions, tetany, and paresthesia [2,6,7]. Saudi Arabia has a high prevalence of vitamin























# Radiological changes of Rickets



# Prevention & Treatment of vitamin D Deficiency



# Prevention of Vitamin D deficiency among children

- Supplementation studies, among healthy people have shown a significant improvement in vitamin D status & bone health.
- Studies have shown vitamin D supplementation decreases and protects against respiratory tract infections in infants and children.
- Vitamin D fortification studies in healthy children were reported. Significant increase in serum calcium & vitamin D levels and also in Bone Mineral Content (BMC) was observed.
- In another study, 776 school children were given fortified milk and significant improvement in their vitamin D status was observed

# Prevention of vitamin D deficiency

- In premature infants, 800 IU of vitamin D & 150-200 mg/kg of calcium are recommended daily.
- In neonates, 400 IU of vitamin D & 200 mg of calcium are recommended daily.
- In infants (after neonatal period) up to 1 year of age, 400 IU of vitamin D/day and 250-500 mg/day of calcium are recommended daily.
- Ages from 1-18 years, 600 IU vitamin D/day and 600-800 mg/day of calcium are recommended daily.



---

### Vitamin D Supplementation (Cholecalciferol)

---

Prevention

400 IU/day

Treatment

1 month: 1000 IU/day orally for  $\times$  2-3 months

1- 12 months: 1000–5000 IU/day orally for  $\times$  2-3 months

12 months: 5000 IU/day orally for  $\times$  2-3 months

---

*IU, international unit*

## Current guidelines for management of Vitamin D deficiency

- For treatment of rickets in premature neonates, infants up to 1 year 1000 IU, 2000 IU & elemental calcium of 70-80 mg/kg/day in premature neonates
- For children 1-18 years 3000-6000 IU of vitamin D daily & 500-800 mg daily for all children over that age are recommended.
- It is recommended that larger doses of vitamin D up to 50,000 IU/week for 8 -12 weeks, then to measure serum vitamin D, if restore to normal to continue on prophylactic doses (especially in communities with low sun exposure).

# Conclusions

- Vitamin D deficiency is incredibly common & most people are unaware of it.
- Symptoms are often subtle & non-specific.
- Advisable, all age groups to screen for its deficiency.
- Fortunately, a vitamin D deficiency is usually easy to be treated.
- Highly advisable, increase people awareness for its deficiency and broadcast preventive measures such as, either increase sun exposure, consume more of vitamin D fortified food / formulas, fish & salmon or fortified dairy products.
- Encourage either sun-exposure (15 -30 minutes per day (longer with darker skin) or vitamin D supplementations.
- The recommended daily intake (RDI) is usually 400–800 IU, but many experts advise to have up to 1000 unit/day.

**Thank you**