Plant Archives Volume 20 No. 2, 2020 pp. 5091-5099 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

VITAMIN D DEFICIENCY AND ITS RELATION WITH SOME DISEASES: A REVIEW

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Abstract

Vitamin D is fat soluble vitamin synthesis from isoprenoid units by condensation process in vivo when exposure to sun light (weak UV source). The main function of vitamin D is maintenance on calcium hemostasis, beside this function has important role as a protection factor from many disease such as autoimmune diseases and cancer. There are several suggestions to support the immunity such as intake vitamin D that has the ability to reduce the risk of respiratory tract infections, such as epidemiology of influenza and COVID-19. Vitamin D can reduce the risk of COVID-19 infection through the mechanisms including lowering replication of virus by induction of cathelicidins and reduced the inflammatory cytokines that produced from the lining cells of lungs which lead to pneumonia and lung fibrosis due to autoimmune diseases as well as increase the concentrations of anti-inflammatory cytokines.

Key words: Vitamin D, COVID-19, cancer, autoimmune diseases, calcium hemostasis

Introduction

Vitamin D from the fat soluble vitamins serve as prohormone because can synthesis in the body when exposure to ultraviolet light at wavelength (290-315) nm from its precursors (7-dehydrocholesterol) (Brannon *et al.*, 2008). Vitamin D useful to conserve of many of biological functions such as metabolic and reproductive process, muscular, skeletal, cutaneous, respiratory and immune systems of men and women at any age stage (Wolf *et al.*, 2007)(Inaguma *et al.*, 2008). therefore according to researchers reports the lower levels of 25-hydroxyvitamin D [25-(OH)D] associated with risk for bone fractures (Al-Aly, 2007)(Dobnig *et al.*, 2008), falls (Melamed *et al.*, 2008), cardiovascular diseases (Autier, Gandini and Mullie, 2012), colorectal cancer (Judd and Tangpricha, 2008), diabetes mellitus (Mathieu *et al.*, 2005), depression (Sloka, Grant and Newhook, 2010), cognitive decline (Mathieu *et al.*, 2004).

Vitamin D deficiency (VDD) can be determined by measuring concentration of serum 25-(OH)D. From the difficulties in measurement of 25-(OH)D levels is presence of multiple assays (Prince *et al.*, 2008), and lack of an international reference for measurements of vitamin D (Broe *et al.*, 2007). Recently, the Ministry of Health and Cancer Society of New Zealand (Bischoff-Ferrari *et al.*, 2009), Institute of Medicine (Osborne and Hutchinson, 2002) and American Academy of Dermatology (AAD) and AAD association (Freedman *et al.*, 2007) they are agree on the minimum concentrations of 25(OH)D at least 50 nmol/L for better healthy cases. VDD is common in regions and countries of North America, Northern Europe, Saudi Arabia, the UAE, Australia, Turkey, Iraq, and Lebanon (Freedman *et al.*, 2007).

A lot of studies have been illustrate VDD is associated with elevated levels of serum Parathyroid Hormone (PTH) due to indicative effect of secondary hyperparathyroidism (Garland *et al.*, 2006). Also, low of vitamin D levels may be related with several factors include darker skin (pigmentation) (Heaney, 2008), lower intake of vitamin D (Ebers, 2008), insufficient exposure

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to sun light (Kampman, Wilsgaard and Mellgren, 2007)(Willer *et al.*, 2005), obesity (van der Mei *et al.*, 2003), Older age (Holick, 2004), and female sex (Adorini and Penna, 2008), no sport exercise (Szodoray *et al.*, 2008), and bad health status (Munger *et al.*, 2006).

Vitamin D deficiency treatment by increase intake of vitamin D rich foods and in severe deficiency give the patients oral vitamin D in several forms (tablet or gel capsule) dosage (200-500 IU), in some times can be given in combination with calcium (Kragt *et al.*, 2009)(van der Mei *et al.*, 2007). The side effect of hyper dosage of vitamin D hypercalcemia, hyperphosphatemia, suppressed parathyroid hormone levels, and hypercalciuria (Soilu-Hänninen *et al.*, 2005)(Al-Mahdawi, Al Gawwam and Al Ethawi, 2014). The following table show some studies related with vitamin D.

Vitamin D Deficiency as a Risk Factor for Infected by COVID-19

The world is in the hold of the COVID-19 pandemic. There are several suggestions to support the immunity such as intake vitamin D that has the ability to reduce the risk of respiratory tract infections, such as epidemiology of influenza and COVID-19. Vitamin D can reduce the risk of COVID-19 infection through the mechanisms including lowering replication of virus by induction of

Author	Project	Year	Reference
Sarah A. Stechschulte *et al.*	Vitamin D and bone relation diseases	2009	(Stechschulte, Kirsner and Federman, 2009)
Daniel Bikle *etal*	Vitamin D metabolism and clinical significance	2008	(Bikle, Adams and Christakos, 2009)
Wolpowitz D and Gilchrest BA	Vitamin D dosage	2006	(Wolpowitz and Gilchrest, 2006)
Simonelli C *et al.*	Vitamin D and related with trauma	2005	(Simonelli *et al.*, 2005)
Rapuri PB *et al.*	The levels of Vitamin D in summer and winter	2004	(Rapuri, Gallagher and
			Haynatzki, 2004)
Plotnikoff GA and Quigley JM	Severe deficiency of vitamin D in the patients with muscles pain	2003	(Plotnikoff and Quigley, 2003)
Merlino LA *et al.*	Vitamin D and rheumatoid arthritis	2004	(Merlino *et al.*, 2004)
Chiu KC *et al.*	Vitamin D and insulin resistance	2004	(Chiu *et al.*, 2004)
Bulliard JL	Vitamin D and cancer	2000	(Bulliard, 2000)
Gallagher RP and Lee TK	Vitamin D and ultraviolet exposure	2006	(Gallagher and Lee, 2006)
Zittermann A *et al.*	Cardiovascular diseases and vitamin D	2005	(Zittermann, Schleithoff and Koerfer, 2005)
Langman CB and Brooks ER	Renal diseases in children and related with vitamin D	2006	(Langman and Brooks, 2006)
Linhartova K *et al.*	Parathyroid hormones and vitamin D	2008	(Linhartová *et al.*, 2008)
Watson KE *et al.*	Coronary calcification and vitamin D	1997	(Watson *et al.*, 1997)
Marks R *et al.*	Sun exposure and vitamin D	1995	(Marks *et al.*, 1995)
Thomas MK *et al.*	Medical inpatients and vitamin D deficiency	1998	(Thomas *et al.*, 1998)
Holick MF	Health complications and vitamin D deficiency	2006	(Holick, 2006)
DeLuca HF	Story of vitamin D	1988	(DeLuca, 1988)
DeLuca HF	Physiology and metabolism of vitamin D	1984	(Deluca, 1984)
Holick *et al.*	Evaluation and treatment	2011	(Holick *et al.*, 2011)
Norman, A.W.	Vision and vitamin D	2010	(Norman and Bouillon, 2010)
Sergeev I.N.	Vitamin D and Obesity	2014	(Sergeev, 2014)
Song Q. and Sergeev, I.N.	Obesity in vitamin D and calcium deficiency	2012	(Song and Sergeev, 2012)
D. Cashman *et al.*	Vitamin D deficiency in Europe: pandemic?	2016	(Cashman *et al.*, 2016)
L. M. De Regil and *et al.*	Vitamin D supplementation for women during pregnancy	2016	(De Regil *et al.*, 2016)

Table Continued ....

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M. F. Holick	The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention	2017	(Holick, 2017)
P. Lips *et al.*	Vitamin D and type 2 diabetes	2017	(Lips *et al.*, 2017)
R. Scragg *et al.*	Effect of monthly high-dose vitamin D supplementation on cardiovascular disease in the vitamin D assessment study: a randomized clinical trial	2017	(Scragg *et al.*, 2017)
A. R. Martineau *et al.*	Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data	2017	(Martineau *et al.*, 2017)
L. J. P. Staniszewski *et al.*	Assessment of Novel Vitamin D Receptor Antagonists that Mediate Suppression of Vitamin D Signaling	2018	(Staniszewski *et al.*, 2018)
E. M. Mowry *et al.*	Body mass index, but not vitamin D status, is associated with brain volume change in MS	2018	(Mowry *et al.*, 2018)
A. Gil *et al.*	Vitamin D: classic and novel actions	2018	(Gil, Plaza-Diaz and Mesa, 2018)
G. Bakris and M. Sorrentino	Vitamin D Life	2018	(Bakris and Sorrentino, 2018)
J. E. Manson *et al.*	Vitamin D supplements and prevention of cancer and cardiovascular disease	2019	(Manson *et al.*, 2019)
D. A. Jolliffe *et al.*	Adjunctive vitamin D in tuberculosis treatment: meta-analysis of individual participant data	2019	(Jolliffe *et al.*, 2019)
M. Pereira Santos *et al.*	Polymorphism in the vitamin D receptor gene is associated with maternal vitamin D concentration and neonatal outcomes: A Brazilian cohort study	2019	(Pereira Santos *et al.*, 2019)
C. F. Garland *et al.*	Sunlight, vitamin D, and mortality from breast and colorectal cancer in Italy	2019	(Garland *et al.*, 2019)
S. Bouffar	The efficacy of Vitamin D as adjunctive treatment of Chronic Obstructive Pulmonary Disease	2020	(Bouffard, 2020)
E. Wesselink *et al.*	Chemotherapy and vitamin D supplement use are determinants of serum 25-hydroxyvitamin D levels during the first six months after colorectal cancer diagnosis	2020	(Wesselink *et al.*, 2020)
P. E. Marik *et al.*	Does vitamin D status impact mortality from SARS-CoV-2 infection?	2020	(Marik, Kory and Varon, 2020)
E. Von Mutius and F. D. Martinez	Vitamin D Supplementation during Pregnancy and the Prevention of Childhood Asthma	2020	(Von Mutius and Martinez, 2020)
W. B. Grant *et al.*	Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths	2020	(Grant, Lahore, McDonnell, *et al.*, 2020)
M. J. Bradshaw *et al.*	Vitamin D and Multiple Sclerosis	2020	(Bradshaw, Holick and Stankiewicz, 2020)
A. Panarese and E. Shahini	Covid 19, and vitamin D	2020	(Panarese and Shahini, 2020)

cathelicidins and reduced the inflammatory cytokines that produced from the lining cells of lungs which lead to pneumonia and lung fibrosis due to autoimmune diseases as well as increase the concentrations of anti-inflammatory cytokines. From the evidence on the protective effect of vitamin D against COVID-19 is increase the number of patients that infected in the winter due to a decrease in the concentration of this vitamin to its lower levels and as well as the deficiency of vitamin D with older age and who have acute respiratory distress syndrome or chronic diseases. So, to minimize the risk of completions or infections, recommended for a people to intake 10,000 IU of vitamin D for a few weeks followed by 5000 IU to quickly elevated vitamin D level and reach to 40-60 ng/ml (100-150 nmol/l) (Grant, Lahore, Mcdonnell, *et al.*, 2020).

Vitamin D Deficiency Correlation with Multiple Disorders

Vitamin D has several benefits for organism, therefore it is deficiency related with various osteoporosis due to calcium imbalance, as well as in cancer, ischemic heart diseases, diabetes, autoimmune and infectious diseases. Also increase skeletal disorders, such as elevated levels to incidence of malignancies, colon cancer, prostate and breast gland cancer (Peterlik and Cross, 2005).

The following we will discuss the eight disorders in more details as related with VVD.

Heart Disease

Monitoring levels of vitamin D in the people suspected to incidence of heart diseases is important due to correlation between them as increase risk factors such as (hypertension and diabetes) because vitamin D is related with electrolytes levels, so the patients with hemodialysis is more probability to become heart failure (Al-Kufaishi, 2015).

Evidence suggests so higher plasma concentrations on 25-hydroxy vitamin D may also minimize the gamble of hypertension (Gröber *et al.*, 2013). Some meta analyses have recommended a gore pressure lowering effect concerning diet D supplementation, whilst other meta-analyses, into 2015, should no longer confirm these findings then confirmed no impact on vitamin D supplementation on blood pressure (Judd and Tangpricha, 2009). Further, in a recent randomized controlled trial of 200 hypertensive patients, no giant impact concerning vitamin D supplementation of 24 h gore stress could keep performed (Drechsler *et al.*, 2010).

In addition vitamin D have suppression effect to the gene that unregulated in myocardial hypertrophy (Beveridge *et al.*, 2015). Also , regulate1, 25-dihydroxy vitamin D might have been demonstrated to push antihypertrophic. Impacts around cardiomyocytes Furthermore decreased the outflow of a few genes. Which are unregulated Previously, myocardial hypertrophy (Al-Dujaili, Munir and Iniesta, 2016). Concealment. Of the cardiovascular Renin-Angiotensin framework (RAS) also of natriuretic peptides might incompletely intervene these antihypertrophic impacts for vitamin D. Separated starting with this; vitamin D exerts Different impacts on the development Also. Separation for cardiomyocytes. Person valuable enter component of. Vitamin D may be will restrain unreasonable burgeoning from claiming cardiomyocytes (Chen *et al.*, 2011). Pilz *et al.* Elucidated if insufflate vitamin D status is connected with heart disappointment Furthermore sudden demise cardiovascular passing.

Real finding of the contemplate might have been that low levels for 25-hydroxy vitamin D Also 1,25-dihydroxy vitamin D were connected with predominant. Myocardial dysfunction because of heart failure (Chen *et al.*, 2011).

Those low pervasiveness from claiming patients with extreme vitamin D insufficiency Also. Those generally short medicine period show up with be those limits. For this consider as writers were unabated will avoid noteworthy impacts about (Al-Kufaishi, 2016). Vitamin D clinched alongside populaces with low vitamin D levels and for longer. Medicine or diverse doses about vitamin D. It is be noted that the point when supplementing vitamin D, it as a rule takes about 3 months will achieve a enduring state to circle 25-hydroxy vitamin D concentrations; Be that as. In this study medicine time might have been moderately short, which expands those. Segregation racial inclination for effects (Pilz *et al.*, 2015).

Pilz *et al.* performed in turn ponder for those point will gatherings give. A review of the pathophysiological instruments and the. Epidemiological information concerning vitamin D lack What's more myocardial. Sicknesses (Pilz *et al.*, 2010). A few body of evidence reports highlight pediatric cardiomyopathies, which are connected with vitamin D lack or rickets (Elidrissy, Munawarah and Alharbi, 2013)(Elidrissy, Munawarah and Alharbi, 2013). All the more. Importantly, kids with vitamin D insufficiency connected heart disappointment. Indicated By and large An huge clinical change after vitamin D Also calcium supplementation (Fanari *et al.*, 2015). A post mortem examination of a. Child, who kicked the bucket because of vitamin D insufficiency connected cardiomyopathy. Indicated an expansive pericardial radiation Furthermore an developed heart for An widened. Furthermore concentric hypertrophic left ventricle. There might have been An gentle build. For interstitial stringy tissue, especially in the subendocardial districts. And the cardiomyocytes were dainty and lengthened clinched alongside keeping with widened cardiomyopathy (Kienreich *et al.*, 2013).

Zittermann *et al.* Discovered fundamentally diminished 25-hydroxy vitamin. D What's more 1,25-dihydroxy vitamin D levels over 54 heart disappointment patients. At compared with 34 age, sex, What's more BMI-matched controls (Ajabshir, Asif and Nayer, 2014).

For An investigation Around 102 African Americans, vitamin D insufficiency might have been. Watched On 84-96% of heart disappointment patients, while main one-third. Of the sound controls were vitamin D insufficient (Teotia and Teotia, 2008). Two All the more. Investigations "around African Americans Additionally indicated a secondary predominance of. Vitamin D lack done patients for heart disappointment. Interestingly, not. The sum heart disappointment patients for vitamin D lack show elevations in. PTH levels, Be that the individuals with optional hyperparathyroidism need more. Extreme types of heart disappointment (Mitri and Pittas, 2014).

In the national wellbeing Furthermore sustenance examination study. (NHANES), An population-based ponder in the us including 8351. Persons, 25-hydroxy vitamin D levels were fundamentally decreased Previously,. Patients with self-reported heart disappointment with those most noteworthy predominance for. Vitamin D insufficiency clinched alongside patients enduring from both, coronary heart. Illness What's more heart disappointment. In this study, low 25-hydroxy vitamin D. Levels were connected with more extreme congestive heart disappointment Furthermore. For impeded exercise ability. Clinched alongside An companion of over 3,000 patients. Alluded for coronary angiography, 25-hydroxy vitamin D and additionally. 1,25-hydroxy vitamin D were conversely associated for cleared out ventricular. Brokenness (Martineau and Jolliffe, 2014).

Outcomes starting with An investigation "around 150 patients with congestive heart. Disappointment What's more 150 age, sex, Furthermore race-matched controls indicated that lifestyle. Components connected with low 25-hydroxy vitamin D levels On prior. Life (childhood, adolescence, Furthermore adulthood) including home. To substantial towns, low physical activity, and low recurrence about summer camp. Occasions were essentially additional basic clinched alongside heart disappointment patients over. Previously, controls (Goldsmith, 2015).

A prospective ponder to which 3299 patients alluded to coronary. Angiography discovered that low 25-hydroxy vitamin D and also.

Cardiovascular danger figures connected with an expanded hazard from claiming demise. Because of heart disappointment What's more for sudden demise cardiovascular passing (Goldsmith, 2015) (Tordoff, 2001). Furthermore,. Low1,25-dihydroxy vitamin D concentrations were associated with increased mortality in 510 patients from a specialized heart center and were an independent predictor of death and the need for cardiac transplantation in 383 end-stage congestive heart failure patients (Mithal *et al.*, 2014).

Bone Defect

Vitamin D play important role in bone maintenance, because its prevent several chronic diseases as ostateomalacia and rickets beyond osteoporosis (Sunyecz, 2008). Although calcium level within normal value, but calcium hemostasis disturbed due to VVD (McKay *et al.*, 2009) (Pilz *et al.*, 2013). A low level of vitamin D associated with osteoporosis is unclear (Pilz *et al.*, 2013). One from the responsible mechanism to investigate osteoporosis is regulatory effect of vitamin D to parathyroid hormone, which responsible about calcium hemostasis (Adams and Hewison, 2012).

Vitamin D and Cancer

In 2009 the National Cancer Institute represented vitamin D reduced the possibility to cancer incident such as prostate, breast, and other malignancy (Donaldson, 2004). This effect occur by inhibiting cell proliferation by vitamin D receptor (VDR) (Sun, 2010). Also, through inhibiting gene that responsible about cancer by polymorphism process (Dusso, 2011).

Immunological Role of Vitamin D

Vitamin D act as potent modulator for immunological cell as macrophage, B-cells, and T-cells (Hyppönen *et al.*, 2000). Therefore the low levels of vitamin D lead to impairment for macrophage activation, and function to prevent infectious diseases (Zerwekh, 2008).

VVD increase the risk for autoimmune diseases as rheumatoid arthritis, SLE, multiple sclerosis and type I diabetes (Bacon *et al.*, 2010).

Conclusion

In brief, vitamin D has multifunctional inside human body. Therefore must be monitoring his levels by biochemical tests. The lower levels of vitamin D association with several diseases such as cardiac, autoimmune and bone diseases. The oral administration of vitamin D capsule 400 IU per day to protect people from risk infected by COVID-19. Whereas the numerous experiments for a clinical trial reported a vitamin D supplementation could reduce the risk of influenza.

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