MINI REVIEW

Prevalence and correlates of vitamin D deficiency-perspectives from Pakistan

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Abstract: Health outcomes of vitamin D deficiency (VDD) are beyond rickets, osteomalacia, osteoporosis, falls and fractures and have now touched the boundaries of CVD, diabetes and many types of cancer. Therefore, thinking of mere dependence on the sun to meet vitamin D requirements under the existing set of conditions is erroneous. Pakistan as a developing economy of South Asia and a region spanning latitude 24° 35' North and longitude 61° East to 78° East, gravely suffers from increased VDD among pregnant women, neonates, infants, children, adolescents, adults, and the elderly people despite its abundant sunshine. Multiple indicators inflating VDD have been widely reported such as food habits, sociocultural and religious taboos, restricted sun exposure, unavailability of fortified diets, age, season, gender, lack of vitamin D supplementation, skin pigmentation and genetic factors. Strategies entailing mandatory food fortification, pragmatic implementation of vitamin D supplementation program, developing awareness on health damaging effects of the syndrome and sagacious sun exposure in tandem with global support to incline the government, program managers and consumers, need to be followed. Concerted efforts are further required to scale up the surveillance and monitoring of the magnitude of VDD by taking NGOs, industry, academia and health sector into loop to devise remedies for VDD in Pakistan.

Keywords: Vitamin D, 25 (OH) D, Pakistan.

INTRODUCTION

Vitamin D, a fat-soluble vitamin, is physiologically produced subcutaneously from 7-dehydrocholesterol as a result of exposure to ultra violet light (wavelength 290-315nm). Subcutaneous photosynthesis of vitamin D primarily depends upon a multitude of factors including latitude, time and duration of sun exposure, pollution, skin pigmentation, religious taboos, genetic factors and clothing. 25-hydroxyvitamin D [25(OH)D], circulating form of vitamin D in the body, is generally considered as a marker for vitamin D status of the individuals (Londhey, 2011; Holick, 2003). Cut off values for serum 25(OH) D level to define VDD and insufficiency for various age groups vary geographically for several reasons including sunexposure and dietary habits. Numerous groups of researchers defined25 (OH)D <20ng/ml ascut-off forvitamin D insufficiency and VDD among children and adults (Holick, 2007; El-Hajj Fuleihan and Vieth, 2007).Similarly, serum 25(OH)D level of <10ng/ml was reported as cut off for VDD by Lips, (2007). These serum 25(OH)D cut-off levels may differ on the basis of season, ethnicity and the region e.g. serum 25(OH)D level of 30 ng/ml and 10ng/ml have been established as cut-off for adequacy and deficiency respectively in South Asian regions while serum 25(OH)D 15ng/ml were widely used as cut-off for VDD in Europe (MacFarlane *et al.,* 2004; Tangpricha *et al.,* 2002). In the face of enormous discussions on cut-off values for serum 25(OH)D level in foregoing studies, global scientific community defined serum 25(OH)D level of 20ng/ml with a consideration to raise it to 32.05ng/ml for sufficiency and optimal health however, these values for serum 25(OH)D level were shown to contradict with those suggested by Holick (2006) i.e. 25(OH)D<20ng/ml as VDD and <30ng/ml as vitamin D insufficiency. In Pakistan, experts have widely used serum 25(OH) D<8ng/ml as vitamin D deficiency, 21-29ng/ml as vitamin D insufficiency and > 30ng/ml as vitamin Dsufficiency (Bhatty *et al.,* 2010).

Osteomalacia, a disease of defective bone mineralization, has been shown to be a consequence of severe serum 25(OH)D deficiency (Prentice, 2008). Low levels of 1, 25(OH) vitamin D have also been found to be associated with a variety of syndromes e.g.a high prevalence of 25(OH)D deficiency is known to exist among patients suffering from chronic kidney disease which is shown to get worsened with progression of kidney disorder (Dusso *et al.,* 2011; Kim *et al.,* 2011; Holick 2005).Vitamin D deficiency seems to negatively impact diabetes and blood pressure, CVD and other chronic illnesses (Ahasan and Das,2013). Cancer resurgence and compromised immune function leading to tuberculosis, have been reported in patients with depleted vitamin D levels. Other physiological threats associated with low vitamin D levels such as HIV, asthma, reduced hair growth and high

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triglyceride levels have also beendocumentedin the literature and supplementation seems to show no effect against these conditions (Nnoaham and Clarke, 2008; Paul *et al.,* 2012; Elena *et al.,* 2011; Amor *et al.,* 2010).

Compelling evidence suggests occurrence of nutritional rickets as a result of severe deficiencies of calcium or vitamin D, or a combination of milder deficiencies of both. Presence of vitamin D receptors (VDR) in most of the body cells, possessing the ability to form 1,25(OH)2D3 has opened new avenues with respect to their potential role in regulating certain genes. These genes have been shown to be involved in cell growth thus rebuilding the paradigm on vitamin D's role from musculoskeletal and bone health to the prevention of several forms of cancer, including breast, colon, and prostate (Mitchell, 2011; Petti for, 2004).

Worldwide prevalence of vitamin D deficiency or insufficiency accounts for 1 billion people (Holick, 2007) and the situation is more precarious in developing countries of South Asia. Nearly, 6-70% population in Southeast Asia and 70% in South Asia have been affected by VDD (Nimitphong *et al.,* 2013). Amongst resource constrained South Asian societies, Pakistan occupies a larger share of vitamin D deficient population in addition to India where poverty and malnutrition continue to prevail and exacerbate the magnitude of VDD. For example, estimates indicate 84% of pregnant women in India and 70% of healthy volunteers in Pakistan are distressed by VDD. Sri Lanka and Bangladesh are no exception where 26% of male children and 8% of children are the victims of VDD respectively (Akhtar, 2013). VDD remains to be neglected in Pakistan as an issue of public health significance for a number of reasons important being limited dietary intake of vitamin D, inappropriate exposure to sunlight for maintaining optimal levels of 25(OH)D in tandem with several sociocultural and economic determinants (Akhtar *et al.,* 2013a; Akhtar, 2013). The review in hand is an attempt to assimilate the facts and figures to spotlight current vitamin D status of various population groups in Pakistan. The review also sheds light on significant socioeconomic and cultural indicators for VDD and further provides certain pragmatic approaches to modulate the sunshine vitamin deficiency in Pakistan.

Prevalence of vitamin D deficiency in Pakistan

Establishing cut off values for serum 25(OH)D levels to define vitamin D sufficiency, insufficiency and deficiency remains to be a conundrum however numerous studies elaborated 25 (OH)D <20ng/ml as VDD. Taking these values as standard, the prevalence of VDD was reported to be nearly 70% in South Asia. There have been several reports and surveys manifesting wide spread vitamin D and micronutrient deficiencies among various population fractions in Pakistan, a country with tremendous geopolitical significance in Asia (Akhtar *et. al.,* 2013a). VDD has been generally manifested by the magnitude of the onset of osteomalacia in adults and rickets among children. Illiteracy and gender discrimination are common features among Pakistani population especially in mountainous areas such as Kohistan and Hazara districts. Consequently, increased VDD as manifested by higher prevalence of osteomalacia has been recognized in these areas. Multiple contributory factors responsible for growing VDD prevalence include heavy clothing, limited exposure to sun and reduced dietary intake of vitamin D rich foods (Sahibzada *et al*., 2004; Siddiqui and Rai, 2005).

The gravity at which osteomalacia would prevail in a particular region is not easy to assess as the problem is asymptomatic in adults and mostly goes unnoticed however, prevalence of rickets also represents osteomalacia to be existing in a particular area (Prentice, 2008). Several groups of researchers demonstrated high prevalence of osteomalacia in Pakistani women (Herm *et al.,* 2005; Shahibzada *et al.,* 2004). Clinical osteomalacia has particularly been seen among pregnant and lactating women. However, ample evidence is available to suggest prevalence of VDD among healthy volunteers as well as ambulatory patients in hospital settings of Karachi (Lubna *et al.,* 2008).

VDD gravely affects menopausal females owing to insufficient calcium and vitamin D intake thereby resulting in rapid bone loss. In one study, the researchers reported a close association between bone mineral density and the concentration of serum 25(OH)D among a group of 140 postmenopausal women, suggesting VDD and reduced calcium intake to be the potential markers for osteoporosis (Lowe *et al.,* 2011). Anterior tibial tenderness as a diagnostic tool for VDD among premenopausal women, was explored in Lahore, Pakistan and the upshots of the study confirmed elevated vitamin D_3 level and decreased parathyroid hormone (PTH) on supplementing 1.8 million units of vitamin D_3 in divided doses as compared to control group (Ali *et al.,* 2013; Dar *et al.,* 2012). Khan *et al.,* (2012) demonstrated high prevalence (90.1% of 305) of VDD among premenopausal females in Karachi linking the incidence of VDD to age and living style.

Gauging magnitude of vitamin D deficiency and insufficiency in population groups in Pakistan generally remains to be a demanding task because vitamin D deficient individuals are largely asymptomatic. For example, one study demonstrated 66.32% and 22.62% of the total tested samples (579) drawn from healthy individual were shown to have mild and moderate VDD respectively with cut off value <30ng/ml vitamin D3.The authors were of the opinion that Pakistani population in general suffer from VDD and vitamin D supplementation

needs to be implemented after clinical evaluation of the population groups to address the issue effectively (Anjum *et al.,* 2013). Likewise, Mansoor *et al.,* (2010) elucidated that 56.9% of healthy adult males and 43.1% adult females of total 123suffered from VDD with a cut off value ≤20ng/ml serum 25(OH)D. More recently, healthy asymptomatic adult population group aged 48 (38-55) years was examined for VDD in Karachi and 84.3% of 300 tested subjects had depleted 25(OH)D levels (<30 ng/ml)(Sheikh *et al.,* 2012). These data are also suggestive of extensive VDD prevalence in almost all parts of Pakistan declaring Pakistani population a vitamin D deficient nation.

Pakistan lacks a precise and effectual health care infrastructure which consequents upon drastic health and economic losses. The disease burden and mortality rate associated with malnutrition among a variety of population groups seemingly remain to be unchanged in the last several years (Akhtar 2013a). Nutritional wellbeing of Pakistani population has never been a priority of the Government, industry and the global organizations and efforts underway to tackle VDD have not yet been effective to mitigate the gravity of the issue. Poor monitoring and surveillance to recognize and quantify the problem of vitamin D deficiency has not been a part of any nutritional program in Pakistan. National Nutritional Survey of Pakistan (2011) portrays a dismal picture of the malnutrition including VDD in Pakistan. Nearly, 85.1% of non-pregnant mothers of index child were reported to suffer from vitamin D deficiency and out of these 87.9% belonged to urban areas and 84.2 % from rural areas. Similar magnitude of VDD among pregnant mothers of index child was reported in the survey showing 86.1% of the tested mothers (86.3% from urban and 86.1% from rural areas) to be affected by VDD (NNS 2011). Therefore, more concerted studies and surveys to ascertain the level of VD Dalongside nutritional interventions are needed to address this issue in Pakistan.

Determinants of vitamin D deficiency

It is generally conceptualized that VDD does not exist among populations from countries with abundant sunshine. This notion does not stand true as sun exposure behaviour greatly differs country wise. South Asian countries are relatively more affected with VDD for several reasons predominant being life style, socio economic and cultural taboos and genetic factors. Plant based diets containing high content of fibre, phosphates and phytates lead to restricted dietary calcium and vitamin D intake thereby depleting vitamin D stores and increasing need for calcium in the body (Khadilkar, 2010).

Abundant literature is available to suggest VDD to be genetic in nature among certain individuals as variation in serum vitamin D levels has been linked with the heritability of vitamin D binding protein (Fu *et al.,* 2009). Similarly, features like skin pigmentation, behavioural responses, and cultural practices have their roots in genetics which subsequently determine the vitamin D status of various populations. For example, dark skin leads to relatively reduced synthesis of cholecalciferolsubcutaneously as a result of the same extent of exposure to UVB light as compared with light-skinned individuals. Likewise the tendency to produce plasma 25(OH)D concentration among elderly people appears to be less than those of young adults (Holick, 2004a).

Observance of veil has been strongly practiced in most of the Islamic countries, which deters body exposure to sun in order to meet vitamin D requirements through UVB light. This kind of cultural and religious habits considerably affect the health status of populations in various parts of the world. Therefore, types of dresses covering face, head, and arms, and using sun block have been known to be established reasons for depleted serum vitamin D levels in Muslim countries (Holick, 1994). Populations from Indian sub-continent, practicing different religions indicate differences in serum 25(OH)D levels among males and females due to clothing differences (Mishal, 2001).

Latitude of the country greatly influences vitamin D synthesis among respective population groups. Absorption of UVB is primarily linked with the angle at which sunlight reaches the earth. Vitamin D status may be based on how long and frequent is the body exposure to UVB sunlight taking into account the latitude and season of the region. For locations at latitude below 25°N, UV exposure for longer time is normally considered unsuitable in winter. Despite, Pakistan's location at latitudes 32.0162° N with abundant sunshine throughout the year, VDD remains to be an issue of public health significance. This suggests multiple reasons for the prevalence of vitamin D in Pakistan as the population avails few opportunities for skin sunshine exposure (Akhtar, 2013).

Numerous studies have demonstrated multiple indicators in Asian developing countries including Pakistan for occurrence of VDD such as pollution, inadequate nutritional supplementation and little or no vitamin D fortification of milk and milk products Additionally, rapid urbanization, age, sex and various anthropometric factors, particularly body mass index (BMI) are also important determinants for decreased 25 (OH)D levels in citizens from Asian developing regions (Babu and Calvo, 2010).

Health consequences of vitamin D deficiency

Prevalence of nutritional rickets has been shown to decline in many developed countries. However, nutritional rickets still remains a public health problem

among infants and young children in many Asian developing countries (Pettifor, 2004). South Asian populations have been excessively shown to suffer from rickets for restricted calcium intakes. Estimates show rickets to be one of the five commonest diseases prevailing among children from resource constrained Asian countries. Severe VDD has been reported to result in the development of rickets among infants and is generally presented as hypo mineralization and deformities, muscular weakness, and subsequently growth retardation. Moreover, it was elucidated that sub clinical VDD was a potential marker of high prevalence of rickets among children (Holick, 2006).

Osteoporosis is a consequent effect of advancing age due to increasing rates of bone losses. The syndrome is considered serious owing to its deleterious impact on musculoskeletal health leading to weak and brittle bones. VDD and low calcium intake consequentially engender likelihood of osteoporosis onset. Menopausal females are relatively more prone to the risk due to decreased oestrogen because the hormone stimulates bone remodelling. Similarly, adequate levels of vitamin D among adolescents substantially reduce the risk of osteoporosis in the later years of life. Increased risk of fracture has been strongly associated with VDD because of low bone mass and muscle weakness (Akhtar, 2013). Hyperparathyroidism as an outcome of VDD and low calcium in take, leads to elevated bone turnover and osteoporotic fractures (Riggs, 2003).

Osteomalacia is generally represented in adults as aches and pains in the lower back and subsequently extends to thighs, arms and ribs. The patient shows a typical "waddling" gait (Eisman John, 1988). Decreased levels of vitamin Dhave been associated with this disease resulting in softening of bones due to defective bone mineralisation. This syndrome is exacerbated where amount of phosphorous and calcium are inadequate or overactive resorption of calcium from bone takes place as a result of hyperparathyroidism (Sompura *et al.,* 2014). Several factors have been recognized to contributing towards developing osteomalacia i.e. dietary VDD, kidney failure, liver disorders, phosphate depletion and hereditary disorders of vitamin D metabolism (Mankin, 1990; Pitt, 1991).

Abundant literature is available to demonstrate the possible role of VDD in resurgence of some types of cancer. Hanchette and Schwarz (1992) investigated VDD and its association with prostate cancer. The researchers suggested the high prostate cancer risk in areas with lower UV exposure and decreased vitamin D levels in population groups. Previous investigation established relationship between VDD and cancer by reporting higher mortality in patients with prostate cancer. More recently, presence of vitamin D receptors in the body has opened new avenues to explore the role of VDD in cancer resurgence. These receptors have been shown to be highly expressed in epithelial cells, which are at a risk for carcinogenesis (Welsh, 2012; James *et al.,* 2012). However further research is needed on vitamin D and its association with breast, prostate and colorectal cancers.

CONCLUSIONS

Increased global prevalence of VDD and its health and economic outcomes have raised a major concern to address this issue of public health significance. Developing nations are more predisposed to the damaging effects of VDD for a bulk of reasons including poverty, illiteracy and socioeconomic and cultural behaviour. Pakistan stands at a lower rung of development ladder which necessitates more rigorous local and global efforts to overcome this issue of tremendous health significance. Sufficient data are available in Pakistan to explicit the increased VDD among population groups irrespective of age, sex, physiological and socioeconomic status. Health outcomes of VDD such as rickets, osteomalacia, osteoporosis, CVD and cancer, are drastic and warrant a complete revamping and revitalization of health infrastructure in Pakistan. Diagnosis, surveillance and epidemiological surveys to gauge up the magnitude of the issue need to be typically focused. The paradigm entailing mere dependence upon cutaneous photosynthesis for adequate vitamin D levels, prevailing among common population, health workers and medical practitioners in developing countries does not stand true as VDD has been recognized in a large number of sunny countries of the world. A perusal of the publications in the recent past shows life style changes, availability of vitamin D rich foods, mandatory vitamin D fortification of the foods, vitamin D supplementation programs, sufficient sun exposure, reduced environmental pollution and facilities for inexpensive and accessible diagnosis of VDD would help mitigate the gravity of the prevalence of VDD in Pakistani populations. Further efforts are needed to create awareness among population groups on deleterious health implications associated with VDD and the ways to overpower this issue of public health significance at individual and collective level.

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REFERENCES

Ahasan HN and Das A (2013). Vitamin D deficiency in South Asian populations: A serious emerging problem. *J. Enam. Med. Coll.*, **3**: 63-66.

Akhtar S (2013). Vitamin D status of South Asian populations- risks and opportunities- *Crit. Rev. Food Sci. Nutr*., DOI 10.1080/10408398.2013.807419

Akhtar S (2013a). Zinc status in South Asian population. *J. Popul. Health Nutr.,* **2**: 139-149.

Akhtar S, Ahmed A, Asif A, Ali Z, Riaz M and Ismail T (2013a). Iron Status of Pakistani population-Current issues and strategies. *Asia Pac. J. Clin. Nutr.,* **22**: 340-347.

Akhtar S, Ismail T, Sunethra A and Arlappa N (2013). Micronutrient deficiencies in South Asia-current status and Strategies. *Trends Food Sci. Tech.,* **31**: 55-62.

Akhtar S, Ismail, T, Atukorala S and Arlappa N (2013b). Prevalence of vitamin A deficiency in South Asia-causes, outcomes and possible remedies. *J. Popul. Health Nutr*., **31**: 413-423.

Ali B, Butt A, Fatima A, McDonnell ME and Masud F (2013). Tibial tenderness identifies secondary hyperparathyroidism responding to high dose vitamin D in Pakistani Women. *Endocr. Pract.*, pp.1-20.

Amor KT, Rashid RM and Mirmirani P (2010). Does D matter? The role of vitamin D in hair disorders and hair follicle cycling. *Dermatol.,* **16**: 3.

Anjum P, Safder N, Khalid M and Mehboob I (2013). Vitamin D deficiency in Pakistani population. *J. Pak. Orthop. Assoc.,* **25**(1):

Babu US and Calvo MS (2010). Modern India and the vitamin D dilemma: Evidence for the need of a national food fortification program. *Mol. Nutr. Food Res.,* **54**: 1134-1147.

Bhatty SA, Shaikh NA, Irfan M, Kashif SM, Vaswani AS, Sumbhai A and Gunpat (2010). Vitamin D deficiency in fibromyalgia. *J. Pak. Med. Assoc.,* **60**: 949-951.

Dar FJ, Iqbal R, Ghani F, Siddiqui I and Khan AH (2012). Bone health status of premenopausal healthy adult females in Pakistani females. *Arch. Osteoporos.,* **7**: 93-99.

Dusso A, Gonzalez EA and Martin KJ (2011). Vitamin D in chronic kidney disease. *Best Pract. Res. Clin. Endocrinol. Metab.,* **25**: 647-655.

Eisman John A (1988). "6 Osteomalacia". *Baillieres Pract. Res. Clin. Endocrinol. Metab.,* **2**: 125-155.

Elena R, Rosa MO and Liliana G (2011). Vitamin D deficiency is an independent predictor of elevated triglycerides in Spanish school children. *Eur. J. Nutr.* **50**: 373-378.

El-Hajj Fuleihan G and Vieth R (2007). Vitamin D insufficiency and musculoskeletal health in children and adolescents. *Int. Congr. Ser.,* **1297**: 91-108.

Fu L, Yun F, Oczak M, Wong BY, Vieth R and Cole DE (2009). Common genetic variants of the vitamin D binding protein (DBP) predict differences in response of serum 25-hydroxyvitamin D [25 (OH) D] to vitamin D supplementation. *Clin. Biochem.,* **42**: 1174-1177.

Hanchette CL and Schwarz CG (1992). Geographic patterns of prostate cancer mortality. Evidence for a protective effect of ultraviolet radiation. *Cancer,* **70**: 2861-2869.

Herm FB, Killgus H and Stewart AG (2005). Osteomalacia in Hazara District, Pakistan. *Trop. Doct.,* **35**: 8-10.

Holick MF (1994). McCollum award lecture, 1994: vitamin D new horizons for the 21st century. *Am. J. Clin. Nutr.,* **60**: 619-630.

Holick MF (2003). Vitamin D: A millennium perspective. *J. Cell. Biochem.,* **88**: 296-307.

Holick MF (2004). Vitamin D: Importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am. J. Clin. Nutr.,* **79**: 362-371.

Holick MF (2004a). Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am. J. Clin. Nutr.,* **80**: 1678S-1688S.

Holick MF (2005). Vitamin D for health and in chronic kidney disease. *Semin. Dial.,* **18**: 266-275.

Holick MF (2006). High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin. Proc.,* **81**: 353-373.

Holick MF (2007). Vitamin D deficiency. *N. Engl. J. Med.,* **357**: 266-281.

James CF, Marsha D, Robert J and Yan L (2012). Vitamin D and cancer: A review of molecular mechanisms. *Biochem. J.,* **441**: 61-76.

Khadilkar AV (2010). Vitamin D deficiency in Indian Adolescents. *Indian Paediatr.,* **47**: 756-757.

Khan AH, Iqbal R, Naureen G, Dar FJ and Ahmed FN (2012). Prevalence of vitamin D deficiency and its correlates: results of a community-based study conducted in Karachi, Pakistan. *Arch. Osteoporos.*, **7**: 275-282.

Kim HS, Chung W and Kim S (2011). Vitamin D and kidney disease. *Electrolyte Blood Press.,* **9**: 1-6.

Lips P (2007). Vitamin D status and nutrition in Europe and Asia. *J. Steroid. Biochem. Mol. Biol.,* **103**: 620-625.

Londhey V (2011). Vitamin D deficiency: Indian scenario. *J. Assoc. Physicians. India,* **59**: 695-96.

Lowe NM, Ellahi B, Bano Q, Bangash SA, Mitra SR and Zaman M (2011). Dietary calcium in take, vitamin D status, and bone health in postmenopausal women in rural Pakistan. *J. Health Popul. Nutr.,* **29**: 465.

Lubna Z, Aysha HK and Abdul J (2008). Vitamin D deficiency in ambulatory patients. *J. Pak. Med. Assoc.,* **58**: 482-484.

MacFarlane GD, SackrisonJr JL, Body JJ, Ersfeld DL, Fenske JS and Miller AB (2004). Hypovitaminosis D in a normal, apparently healthy urban European population. *J. Steroid. Biochem. Mol. Biol.,* **89**: 621-22.

Mankin HJ (1990). Rickets, osteomalacia and renal osteodystrophy. An update. *Orthop. Clin. North. Am.,* **21**: 81-96.

Mansoor S, Habib A, Ghani F, Fatmi Z, Badruddin S, Mansoor S and Jabbar A (2010). Prevalence and

significance of vitamin D deficiency and insufficiency among apparently healthy adults. *Clin. Biochem.,* **43**: 1431-1435.

Mishal AA (2001). Effects of different dress styles on vitamin Dlevels in healthy young Jordanian women. *Osteoporos. Int.,* **12**: 931-935.

Mitchell D (2011). The relationship between vitamin D and cancer. *Clin. J. Oncol. Nurs.,***15**: 557-560.

Nimitphong H and Holick MF (2013). Vitamin D status and sun exposure in Southeast Asia. *Dermatoendocrinol.,* **5**: 0-1.

Nnoaham KE and Clarke A (2008) Low serum vitamin D levels and tuberculosis: A systematic review and meta-analysis. *Intern J. Epidemiol.,* **37**: 113-119.

NNS (2011). National nutritional Survey Pakistan. Nutrition Wing, Cabinet Division, Government of Pakistan.

Paul G, Brehm JM and Alcorn JF *et al.* (2012). Vitamin D and asthma. *Am. J. Respir. Crit. Care Med.,* **185**:124-132.

Pettifor JM (2004). Nutritional rickets: Deficiency of vitamin D, calcium, or both? *Am. J. Clin. Nutr.,* **80**: 1725S-1729S.

Pitt MJ (1991). Rickets and osteomalacia are still around. *Radiol. Clin. North Am.,* **29**: 97-118.

Prentice A (2008). Vitamin D deficiency: A global perspective. *Nutr. Rev.,* **66**: S153-S164.

Riggs BL (2003). Role of the vitamin D endocrine system in the pathophysiology of postmenopausal osteoporosis. *J. Cell. Biochem.,* **88**: 209-215.

Sahibzada AS, Khan MS and Javed M (2004) Presentation of osteomalacia in Kohistani women. *J. Ayub. Med. Coll. Abbottabad*., **16**: 63-65.

Sahibzada AS, Khan MS and Javed M (2004). Presentation of osteomalacia women. *J. Ayub Med. Coll. Abottabad.,* **16**: 63-65.

Sheikh A, Saeed Z, Jafri SAD, Yazdani I and Hussain SA (2012). Vitamin D levels in asymptomatic adults-A population survey in Karachi, Pakistan. *Plo Sone.,* **7**: e33452. doi:10.1371/journal.pone.0033452).

Siddiqui TS and Rai MI (2005). Presentation and predisposing factors of nutritional rickets in children of Hazara Division. *J. Ayub Med. Coll. Abottabad.,* **17**: 29-32.

Sompura S, Jain R, Pandey A, Gupta AK and Jain P (2014). Osteomalacia: An unusual presentation and a brief overview. *J. Indian Acad. Clin. Med.,* **15**: 69.

Tangpricha V, Pearce, EN, Chen TC and Holick MF (2002). Vitamin D insufficiency among free-living healthy young adults. *Am. J. Med.,* **112**: 659.

Welsh J (2012). Cellular and molecular effects of vitamin D on carcinogenesis. *Arch. Biochem. Biophys.,* **523**: 107-114.