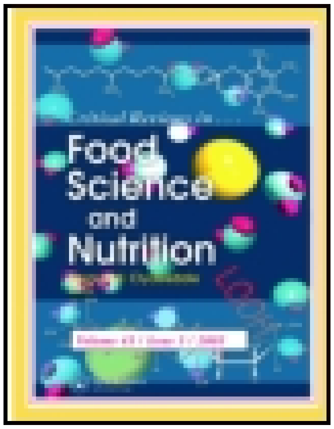

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Vitamin D Status of South Asian Populations- Risks and Opportunities

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Review Article

Vitamin D Status of South Asian Populations- Risks and Opportunities

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Abstract

Human body acquires a significant amount of vitamin D by the cutaneous synthesis under the action of sunlight and less is supplied through nutritional sources. Diversified socio-cultural and economic determinants have been identified that limit the dietary intake of vitamin D and enough distribution of sunlight to maintain optimal levels of 25-hydroxyvitamin D [25(OH)D]. Consequently, the world has witnessed a high prevalence of hypovitaminosis D in resource limited South Asian countries. The purpose of this review is to provide a South Asian

perspective of vitamin D status critically examining India, Pakistan, Bangladesh and Sri Lanka and to shed light on potential determinants (latitude and season, sunshine exposure habits, age and gender, genetic factors) leading to hypovitaminosis D among a variety of population groups. Literature search was carried out using bibliographic databases ñPubMedò, ñGoogle Scholarò and ñScienceDirect.comò.. . Serum 25(OH)D level 20-50 nmol/L was mainly taken as vitamin D deficiency and determinants of low serum 25(OH)D concentration of the population under study were also considered. The review concludes that vitamin D deficiency is highly prevalent among South Asian population and global efforts are needed to overcome hypovitaminosis in the region. Additionally, dietary diversification, supplementation and fortification of foods with vitamin D, adequate exposure to sunlight and consumption of animal foods were suggested as viable approaches to maintain 25 (OH)D levels for optimal health.

Introduction

Calciferol commonly known as vitamin D plays a fundamental role in calcium metabolism and is essentially required to maintain skeletal health. Inadequate intake of calcium and vitamin D provokes the risk of fractures in postmenopausal women with a bone loss of 1ï 2 % every year (Cashman, 2002; Nieves, 2005). The weight of compelling scientific evidence for preventive role of this vital nutrient built scientific consensus on vitamin D implication with major chronic diseases such as hypertension, cardiovascular disease (CVD), cancer and diabetes (Holick and Chen, 2008; Jyrki et al., 2011; Lee et al., 2008; Pittas et al., 2007). Vitamin D mainly exists in two forms i.e. vitamin D_2 (ergocalciferol, produced from ergosterol,) and vitamin D_3 (cholecalciferol, produced from 7-dehydrocholesterol, a precursor naturally occurring in the skin of animals) with a structural difference in their side chains (Holick et al., 2007, 2011; Houghton and Vieth, 2006).

Globally, around one billion people suffer from vitamin D deficiency, attributing this pandemic of hypovitaminosis D to lifestyle (Nair and Maseeh, 2012). Osteomalacia, also named as rickets for children, is characterized by soft bones because of calcium or phosphorus and vitamin D deficiencies, eventually leading to bone mineralization and bone-softening diseases (Grant and Holick, 2005). There is an accumulating body of literature to support the evidence of regional impact on the development of vitamin D deficiency and mortality rates. More distance from the equator with less exposure to UVB radiation from the sun is another surrogate marker of higher cancer mortality in this region (Fleck, 1989; Grant, 2003; Grimes et al., 1996; Mizoue, 2004). Populations from low-income countries of Asia predominantly suffer from vitamin D deficiency (Lerch and Meissner, 2007). Currently, vitamin D deficiency has been found to affect 84% of pregnant women in India, 70% of healthy volunteers in Pakistan, 26% of male children in Sri Lanka and 8% of children in Bangladesh (Akhtar et al., 2013)Diet patterns devoid of meat, fish and eggs, consumption of high extraction cereals, restricted access to milk and milk products and reduced exposure to sunshine are the major determinants for the development of vitamin D deficiency in these regions (Pettifor, 2004).

There are primarily two ways to meet body requirements of vitamin D under normal physiological conditions i.e. dietary intake and cutaneous synthesis resulting from exposure to sunlight. Fatty fish and fish oil are the main reservoirs of vitamin D_3 followed by whole egg, and beef liver. Alfalfa and various edible mushrooms provide significant amount of vitamin D_2 (Anon, 2012; Bouillon et al., 1998; Koyyalamudi et al., 2009). Based on its unique mechanistic supply to human body i.e. synthesis from sunlight, vitamin D is not generally proclaimed as an essential dietary vitamin. What makes it a vitamin is it being an organic compound required as a vital nutrient in a small proportion (Wolf, 2004).

Worldwide recognition of the health significance of vitamin D leads the governments and scientific community to debate the optimal vitamin D status of populations. Fluxes in sunshine exposure, dietary intake, pigmentation, ethnicity and sociocultural and religious taboos predominantly hinder to delineate vitamin D deficiency. Therefore, comparisons are normally made for vitamin D status of populations across the nations depending on thresholds set for hypovitaminosis D. This situation is aggravated due to the visible difference in assays by laboratories for serum 25(OH)D (Lips, 1998; Lips et al., 1999).

Several studies established serum 25(OH)D level of 75nmol/L as the cut-off for adequacy however, in South Asian countries, the vitamin D deficiency is generally defined as 25(OH)D

<25nmol/L with a mean ranging from 10 to 30 nmol/L (Bischoff-Ferrari et al., 2005; Mithal et al., 2009). Cut-off has long been debated and 50 nmol/L for sufficiency was suggested however, a rise to 80 nmol/L has been under consideration by the global scientific community for optimal health (Mithal et al., 2009; Vieth et al., 2007). Contrarily, Holick (2006) suggested 25(OH)D <50nmol/L to be a level indicating vitamin D deficiency and 25(OH)D <75nmol/L as vitamin D insufficiency. Bhatty*et al.* (2010) defined vitamin D deficiency at 25(OH)D<20 nmol/L, vitamin D insufficiency 52.5-72.5 nmol/L and vitamin D sufficiency equal or > 75nmol/L in one of their studies conducted in Pakistan. Most recently (Talaei et al., 2012) cut off values were defined as 25(OH)D<50nmol/L, <37nmol/L and <20nmol/L for mild, moderate and severe vitamin D deficiency respectively, among secondary students of Arak in Iran. Similarly, cut-off points for vitamin D status among South Asian population defined for the purpose of this review are, severe deficiency <20nmol/L, deficiency 20-50 nmol/L, sufficient>50- 75nmol/L and sufficient >75nmol/L (NNS, 2011; Virmani, 2006).

Given the multiple role of vitamin D, it ranks as one of the most neglected vitamins in South Asian low income countries. Vitamin D deficiency was comprehensively reviewed by Virmani (2006) who highlighted the risks and implications of vitamin D deficiency and its squalea. The author explicitly discussed the prolonged vitamin D deficiency as a leading factor to develop osteomalacia/rickets and a variety of associated diseases in developing countries. The role of insufficient intake of dietary vitamin D as another marker of vitamin D deficiency was widely debated in the literature, not supporting the paradox of meeting total vitamin D requirements through mere sun exposure. Later on, another group of investigators reviewed the extent of vitamin D deficiency in various parts of the world, discussing 25(OH)D as a reliable biochemical marker to assess vitamin D levels (Prentice, 2008). Next review was published in 2008 focusing on vitamin D &/or calcium deficiency as the major cause of rickets in infants and children and the authors suggested this nutritional deficiency to be a public health problem particularly in low income developing economies (Pettifor, 2008). The third major review by Mithal*et al.* (2009) precisely depicted the global prevalence of vitamin D, covering Asia, Europe, Latin America, Middle East/Africa, North America, and Oceania and thoroughly discussed the variability in prevalence of vitamin D deficiency with respect to age, gender, ethnicity, latitude, clothing, nutrition, skin pigmentation, cultural practices, and living conditions as potential indicators of vitamin D deficiency. More recently, Nimitphong et al., (2013) reported a high prevalence of vitamin D deficiency (70%) in South Asia while the magnitude of this deficiency varied from 6ï 70% in Southeast Asia. The authors attributed these high vitamin D deficiency to skin pigmentation, aging, lifestyle and nutritional differences. Considerably high magnitude of hypovitaminosis D among South Asian populations might be presumed by a comparison of vitamin D deficiency prevalence in Europe and America due to excessive exposure to sun, pale skin pigmentation and higher vitamin D intakes through supplementation and mandatory fortification which most of the South Asian developing countries lack (Kiely and Black, 2012).

Rampant literature signifies global prevalence of vitamin D deficiency however, data are scant to typically highlight vitamin D status of South Asian populations. The review in hand primarily focuses on the health significance of vitamin D and the extent of prevalence of vitamin D deficiency in India, Pakistan, Bangladesh, and Sri Lanka. This review also gives a thumbnail picture of the causes of vitamin D deficiency with the possible remedies. Fortification, supplementation and modification in dietary patterns have been suggested as potential approaches to control vitamin D deficiency. The reported paradox of the prevalence of rickets and osteomalacia because of restricted sun exposure has been another subject of discussion of this review. Therefore, the article holds the potential to draw the attention of international organizations and allied stakeholders to intervene for the control of this nutritional problem in South Asian developing regions.

Heath Consequences of Vitamin D Deficiency

There are several health implications of hypovitaminosis D including increased mortality (Zittermann et al., 2009). Osteomalacia, rickets and low bone mineral density are known to be the most visible outcomes of vitamin D deficiency along with osteoporosis (Cranney et al., 2007). Furthermore, bone mineralization, secondary hyperparathyroidism, and increased cortical bone loss have been linked to the pathogenesis of osteoporosis and hip fractures (Lips, 2001; Rizzoli and Bonjour, 2004). Currently, a sizable body of literature substantiates vitamin D deficiency association with cardiovascular disease (CVD) however, little is known about the effectiveness of vitamin D supplementation for CVD (McGreevy and Williams, 2011; Pittas et al., 2010), diabetes (Pittas et al., 2007) , and blood pressure (Rostand, 1979). Development of multiple sclerosis and some cancers have also been linked with vitamin D deficiency. Studies confirmed low level of vitamin D to affect immune function resulting in tuberculosis (Cannell et al., 2006). Correspondingly, HIV (Nnoaham and Clarke, 2008), asthma (Paul et al., 2012) and hair growth (Amor et al., 2010) have been directly associated with vitamin D levels and supplementation appears to have little or no effect against these syndromes. Moreover, high triglyceride levels have been reported to result from low serum vitamin D levels in children which could be a greater long term risk of CVD (Elena et al., 2011).

Prevalence of rickets and osteomalacia in South Asia Rickets

Severe vitamin D deficiency leads to rickets among infants and is manifested as skeletal hypomineralization and deformities, muscular weakness, and growth retardation (Holick, 2006). Subclinical vitamin D deficiency in children has been associated with a high prevalence of rickets. Vitamin D deficiency rickets has been reported to exist in many countries of the world in spite of the availability of vitamin D with its demonstrated effect to prevent rickets (Dawodu and Wagner, 2007).

High prevalence of rickets among Indian children has been reported in the literature however, no precise data on vitamin D status of Indian population are yet available (Harinarayan, 2005). Numerous studies confirmed prevalence of rickets in Pakistan e.g. 73.8% of the total children suffering from rickets, reported in one year in Peshawar-Pakistan, were found to be vitamin D deficient (Hameed et al., 1998). Similarly, rickets among malnourished children and children with severe pneumonia existed to 91% and 74 % respectively in the same city. Infants aged 2 to 12 months (79.8%) and breast fed children (85.3%) were found to be more predisposed to rickets (Haider et al., 2010; Khattak et al., 2004).

Amongst several nutritional deficiencies, rickets still remains a public-health problem clinically affecting 8% of children in many parts of Bangladesh (Craviari et al., 2008). Two major surveys conducted by the Helen Keller International in Bangladesh during 2000 and 2004 elucidated rickets to be prevalent among children aged 1-15 years. Similar findings (rachitic deformities in 0.9% of the subjects) were reported by Bangladesh Rural Advancement Committee covering population of Chittagong (Karim et al., 2003). Institute of Child and Mother Health surveyed to assess prevalence of rickets in Chittagong division demonstrating, 8.7% of children to manifest at least one clinical finding suggestive of rickets (Kabir et al., 2004). High consumption of plant based foods with high phytate and low dietary calcium and season are the significant underlying factors for the development of vitamin D deficiency in various age groups in this region (Balasubramanian et al., 2003; Malhotra et al., 2008).

Osteomalacia

The prevalence of osteomalacia is generally hard to measure as the disease is asymptomatic in adults and remains unnoticed in majority of the instances, however, the regions where rickets in children is common, osteomalacia is likely to distress the adults especially pregnant women and the elderly (Prentice, 2008).

India witnesses high prevalence of vitamin D deficiency (Rathi and Rathi, 2011) leading to the occurrence of rickets and osteomalacia. Manifestation of vitamin D deficiency induced osteomalacia dates back to the last century in Northern India (Wilson, 1931) and several renowned researchers and clinicians confirmed regional prevalence of osteomalacia as a clinical syndrome (Marya et al., 1980, 1981; Vaishnava and Rizvi, 1967). One group of researchers determined 25(OH)D level to assess vitamin D deficiency among population in Delhi (Goswami et al., 2000), suggesting the prevalence of vitamin D up to 90 % among the study population. Several other reports (Harinarayan et al., 2007; Marwaha et al., 2005; Sachan et al., 2005) confirmed high prevalence of vitamin D deficiency amongst all age groups in several Indian regions, signifying rickets and osteomalacia to be a problem of public health significance in India. Women from northern parts of India have shown to be gravely afflicted with osteomalacia as compared to other parts and the difference in incidence of osteomalacia is attributed to the availability of solar ultraviolet radiations essentially required for endogenous cutaneous synthesis of vitamin D_3 (Teotia and Teotia, 2008).

Another recent study demonstrated the prevalence of osteomalacia among 79.3 % of the subjects examined by plain radiographs, bone biopsy or isotope bone scan (Chinoy et al., 2011). Additionally, pregnant and lactating women constitute a vulnerable group for vitamin D deficiency and sub clinical osteomalacia in Pakistan (Atiq et al., 1998; Shaheen et al., 2012).

Vitamin D Deficiency in South Asia

Micronutrient deficiencies including vitamin D have been shown to prevail in India, Pakistan, Sri Lanka and Bangladesh, affecting larger segment of the population especially children and pregnant women (Akhtar et al 2013). Amongst several underlying factors for higher prevalence of vitamin D deficiency in these South Asian populations, restricted sun exposure, dietary patterns, and lacking food fortification are significantly important. Exceedingly higher risk of hypovitaminosis D has recently received attention of the scientific community, policy makers and international organizations for serious intervention in low income South Asian developing countries.

Vitamin D deficiency in India

Vitamin D deficiency is widespread among all age groups in various parts of India. Severity of vitamin D deficiency might be well gauged by the data indicating 25(OH)D levels <50 nmol/L in these groups. Several reports confirmed 96% of neonates, 91% of healthy school girls, 78% of healthy hospital staff and 84% of pregnant women suffered from hypovitaminosis D in North India (Arya et al., 2004; Sachan et al., 2005). Air pollution (Agarwal et al., 2002) and urbanizations (Harinarayan et al., 2007) seemed like exacerbating hypovitaminosis D in India.

The situation of vitamin D deficiency is more precarious among pregnant women already suffering from vitamin D deficiency. Restricted dietary calcium intake resulted in reduced trans-placental transport of calcium to the fetus and developed neonatal and infantile rickets in these subjects (Delvin et al., 1986; Purvis et al., 1973)..

Recent studies illustrated vitamin D deficiency to be epidemic in India as 75 % of the study population was affected by vitamin D deficiency [25(OH) D <50 nmol/L] (Shivane et al., 2011). Nearly 76% of pregnant women and women of child bearing and post-menopausal age were shown to suffer from hypovitaminosis D in South India (Harinarayan et al., 2007, 2009; Marwaha and Sripathy, 2008). There have been many other reports on high prevalence of vitamin D deficiency in North India, indicating 16.5% of women of child bearing age and 84% pregnant women affected by vitamin D deficiency (Harinarayan et al., 2011; Marwaha et al., 2011; Puri et al., 2008). Significant female Indian population especially Muslim communities prefer to observe *purdah* (veil) which constitutes a strong basis for no or limited sun exposure and is considered an underlying cause of higher vitamin D deficiency prevalence in India. Therefore, increasing dietary intake of vitamin D in postmenopausal women is beneficial in terms of bone health and to compensate seasonal hormonal variations (Tare et al., 2011; Tenta et al., 2011). Skin pigmentation, inadequate direct sunlight exposure and consumption of low-calcium, high-phytate diets are some of the leading factors for the development of vitamin D deficiency. Mere exposure to sunlight does not seem like befitting to control vitamin D deficiency because darker skin hampers the photosynthesis of vitamin D in the body. Implementation of sagely devised vitamin D food fortification programs at national level is needed as an effective approach to control resurgence of rickets in children and osteomalacia and osteoporosis among vulnerable populations in India.

Vitamin D deficiency in Pakistan

Around 22 studies with sample size ranging from 40-206 were reviewedfor appraisal of the prevalence of vitamin D deficiency in Pakistan and the author remained unsuccessful to catch on any holistic study covering the larger portion of population to assess vitamin D deficiency in Pakistan. Several small studies (Bhatty et al., 2010; Qamar et al., 2011; Sahibzada et al., 2004) illustrated high prevalence of vitamin D deficiency in all age groups, suggesting 95% of the children, 48% of nursing mothers and 52% of breastfed infants to be the victims of vitamin D deficiency in Pakistan (Karim et al., 2011). Foregoing results demonstrated high prevalence of vitamin D deficiency among nursing mothers and their infants after 6 weeks to 11 months of delivery in the upper socioeconomic class. Approximately, 48% of mothers and 52% of infants had vitamin D levels less than 25 nmol/ L. Another study by the same group of investigators confirmed 55% of infants and 45% of mothers manifesting very low serum 25(OH) D levels (<25 nmol/L) in Pakistan (Atiq et al., 1998a,b).

Recent studies conducted to determine the prevalence of vitamin D deficiency among apparently healthy adults, parturients, and pregnant women revealed increased vitamin D deficiency prevalence. A total of 123 subjects comprising 56.9% healthy males and 43.1% females were tested for vitamin D deficiency in Pakistan. Deficiency and insufficiency of vitamin D were defined as 25(OH)D Ò50 nmol/L and 50.1-74.9 nmol/L respectively. Almost, 69.9% of the subjects were found deficient and 21.1% showed insufficient levels of 25(OH)D, suggesting high prevalence of vitamin D deficiency and insufficiency among apparently healthy adults (Mansoor et al., 2010). Another study confirmed 89% of the tested subjects to have desirable vitamin D level [25(OH)D <75nmol/L] (Hossain et al., 2011). Pregnant women in Pakistan are more prone to vitamin D deficiency and insufficiency (Karim et al., 2003). Table 1 indicates recent data presented in National Nutrition Survey Report of Pakistan for the levels of vitamin D deficiency among pregnant and non-pregnant mothers in Pakistan.

Absence of a well-structured and efficient health service system, lack of nutrition education, expensive diagnosis, increased intake of phytate rich foods, limited sun exposure especially in urban areas, and nonexistence of food fortification and supplementation limit the likelihood for controlling vitamin D deficiency in Pakistan. Poor monitoring and surveillance in terms of large scale studies and surveys to ascertain the extent of the magnitude of the prevalence of vitamin D deficiency and implementation of intervention programs for vulnerable groups are needed to address this issue in Pakistan.

Vitamin D deficiency in Sri Lanka

Multiple micronutrient deficiencies are prevalent in various Sri Lankan population factions. Epidemiological studies or surveys typically focusing on the prevalence of vitamin D in Sri Lanka lack to precisely establish vitamin D deficiency however, numerous small studies appear to be a proxy for the vitamin D deficiency in Sri Lanka. For example, one study confirmed serum 25(OH)D< 35 nmol /L among male (26%) and female (25%) respectively (Hettiarachchi and Liyanage, 2010). Similarly another study carried out with a total of 196 participants (30-60 years) in Sri Lanka (7° N), comparing with 242 Sri Lankans (31-60 years) in Oslo, Norway (60° N), depicted a significant heterogeneity in results for serum 25(OH)D. Sri Lankans living in Norway showed 25(OH)D 31·5 nmol/L (deficiency) and those living in Sri

Lanka manifested 54·2 nmol/L (desirable). The study also validated that season had a significant effect on vitamin D status among Sri Lankans living in Kandy and those Sri Lankans living in Oslo, Norway (Meyer et al., 2008). One study assessed bone mineral density (BMD) among preschool children in Sri Lanka reporting serum calcium level to be associated with a change in BMD. The study further confirmed these children as vitamin D deficient. Similarly, children with sufficient vitamin D levels as compared to those with low vitamin D levels (cut-off value for vitamin D < 35.0 nmol/L) were lighter, shorter, and had lower BMD (Hettiarachchi et al., 2011).

Vitamin D deficiency in Bangladesh

Similar to its adjoining states, a significant female population portion in Bangladesh observe veil because of the reason that a majority of the families dislike unveiling even after the marriage. These socio-religious restrictions promote vitamin D deficiency among female population due to restricted exposure to sunshine (Islam et al., 2006). Poverty exacerbates vitamin D deficiency by limiting supply of animal foods in Bangladesh. Given the higher intake of fish, vitamin D deficiency still prevails in the region, implying that several other determinants are also contributory to the prevalence of vitamin D deficiency in Bangladesh. Based on socioeconomic status of women in Bangladesh, the prevalence of vitamin D deficiency [25(OH)D< 37.5 nmol/L] was observed among 38% in high-income group and 50% from low income groups (Ahmed et al., 2012; Islam et al., 2002).

Lactating mothers are at a higher risk of bone loss in Bangladesh because of inadequate dietary intake of vitamin D. Several reports elucidated the prevalence of rickets for the last two decades in Bangladesh. These studies supported the evidence that rickets is more closely related to dietary calcium deficiency (Fischer et al., 1999; Kabir et al., 2004). Therefore, vitamin D and calcium supplementation have been recommended among Bangladeshi children to control the disease (Craviari et al., 2008) Table 2.

Prevalence of Vitamin D Deficiency among South Asian Migrants

Vitamin D levels among populations have been associated with the country of origin, genetic traits, and cultural practices (Mithal et al., 2009). Retrospective studies revealed lower vitamin D levels among immigrants and asylum seekers from Asian countries on living at locations of higher latitude (Arneil 1975; Holvik et al., 2005; Meyer et al., 2004). Several other reports demonstrated population groups of diversified ethnic origins (Middle Eastern, Vietnamese, Asians and African) residing in Europe and Australia to be at much higher risk of developing vitamin D deficiency as compared to their counterparts from European origin (Brock et al., 2004; van der Meer et al., 2006, 2008). Similarly, lower levels of vitamin D were observed among Asian and African young women in Canada as compared to white-Canadian women (Vieth et al., 2001). Ethnicity has been identified as an underlying determinant for the difference in the circulating levels of serum vitamin D which is manifested by skin color and cultural behavior. Evidently, dark skin requires extended sun exposure as compared to light skin for similar levels of cutaneous formation of vitamin D_3 (Clemens et al., 1982; Holick et al., 1981). Vitamin D levels were investigated among several ethnic groups in New Zealand comprising 91% Indians, 6% Sri Lankans and 3% Pakistani of the total participants. The upshot of the study confirmed these groups at higher risk of hypovitaminosis D, attributing vitamin D deficiency to limited sun exposure and consumption of unfortified foods (von Hurst et al., 2009).

A number of representative studies illustrated lower vitamin D status of populations as a result of migration from Asian countries to Europe and North America e,g. populations migrating from Turkey and India to Europe indicated lower vitamin D levels as compared to those residing in Turkey and India (Goswami et al., 2000, 2009; van der Meer et al., 2011). High prevalence of vitamin D deficiency (as measured by plasma 25(OH)D concentration) was seen in another controlled trial of vitamin D supplementation in Asian pregnant women belonging to relatively well-off Asian community in the South of England. The concentration of vitamin D during the last trimester (about 20 nmol/L ,severely deficient) was much lower than those of healthy non-pregnant European population i.e. 25-150 nmol/L in summer and 20-100 nmol/L, in winter (Brooke et al., 1980).

Public Health Significance of Vitamin D Deficiency in South Asia

A plethora of publications in the literature provides ample evidence to suggest that vitamin D deficiency is extensively prevalent in South Asian developing countries. Epidemiological prevalence of vitamin D deficiency in India has been reported (Harinarayan et al., 2011). Pakistani population is no exception to suffer from vitamin D deficiency (Bhatty et al., 2010; Karim et al., 2011; Sahibzada et al., 2004). The dietary patterns lacking vitamin D fortified food of Bangladeshi population significantly contribute to high prevalence of vitamin D deficiency (Ahmed et al., 2012; Islam et al., 2002).

Association of vitamin D deficiency with poorer bone health is now extended to the risk of cardiovascular mortality and various types of cancers such as colon, prostate, and breast, hypertension, and other diseases (Holick and Chen, 2008). In spite of these adverse health effects of vitamin D deficiency, there have been several limitations to establish vitamin D deficiency as a public health priority comparing with vitamin A, iron and iodine deficiencies in South Asian developing countries. Numerous determinants are explicitly attributed to low priority for the reduction of vitamin D deficiency in poorer economies for example, being asymptomatic in nature, vitamin D deficiency is generally not managed in many cases by the medical practitioners. Assuming vitamin D to be a sun-derived vitamin, no vitamin D supplementation is usually recommended. Moreover, diagnosis for vitamin D deficiency is relatively expensive and not much attention is paid to investigate vitamin D deficiency as a cause of several chronic diseases. There is a little awareness, advocacy and compaining on the physiological role and health consequences of vitamin D deficiency as compared to vitamin A, iron and iodine deficiencies in these regions. Since, there is high prevalence of hypovitaminosis D in South Asian communities, therefore local governments should include vitamin D as a micronutrient of public health significance in nutritional plans. Data pertaining to the prevalence of vitamin D deficiency in South Asian countries lack resulting in ineffective policy making to address this issue of public health significance therefore vitamin D deficiency continues to affect a large number of children in South Asia (Akhtar et al 2013). Moreover, it seems appropriate to include elimination of vitamin D deficiency in the priority agenda to achieve Millennium Development Goals for South Asian developing countries. Besides, global efforts are particularly needed to highlight the gravity of prevalence of this nutritional problem and its health implications in these regions.

Determinants of Vitamin D Deficiency in South Asian Developing Countries

Inadequate vitamin D status is a widespread problem among populations dwelling at higher latitudes where higher dose of UV comparing with erythemal UV is required for the synthesis of same amount of vitamin D. Levels of vitamin D synthesis in winter at latitude <25° N compares with those in summer at higher latitude locations because vitamin D UV levels in winter are normally parallel to summertime levels (Genuis et al., 2009; Holick, 2005; Kimlin et al., 2007).

India, Pakistan, Bangladesh and Sri Lanka are located at latitudes 21.7679° N, 32.0162° N 23.8511° N and 7.5653° N respectively. . Latitude and the amount of vitamin D UV create an inverse trend for photosynthesis of vitamin D viz latitude increases, vitamin D UV decreases dramatically. At lower latitude locations (<25°N) UV exposure during winter is unsuitable for extended time. The authors concluded that the wintertime vitamin D UV levels equate summertime levels at low latitudes. Similarly, season of the year has shown to gravely impact the levels of vitamin D production in humans e.g. availability of vitamin D from the sun is limited for larger part of the year at certain latitudes outside of the tropics. Based on latitude of the South Asian countries, it is expected that vitamin D_3 synthesis takes places round the year, however this varies with season due to variation in ultraviolet B irradiance (Bachelet et al., 1991; Kimlin et al., 2007). Abundant literature confirmed the association of the time of the day with optimal vitamin D synthesis in the body. Early and late day especially in winter may not be producing vitamin D more efficiently as compared to peak UVR (deGruijl, 2011; Diffey, 2010; Reeder et al., 2012).

. Low intake of calcium and vitamin D rich foods and the diets with phosphates and phytates are attributed to decreased 25(OH)D concentration (Khadilkar, 2010). Comparing with the developed economies such as the USA and Canada where vitamin D fortification of several foods especially milk is common, South Asian countries are still lagging behind to follow such approaches to prevent vitamin D deficiency. The speculation that adequate sunshine in these regions suffices to meet populationsô requirements for vitamin D, does not stand valid as numerous limiting factors are in place such as observing veil, limited exposure to sun in the urban areas and lifestyles. Micronutrient fortification of foods has been gaining popularity in these areas with special focus on vitamin A, iron and iodine however, vitamin D continues to be a neglected micronutrient. Moreover, dietary guidelines for indigenous foods to achieve optimum intake of calcium and vitamin D need to be formulated as an approach to address vitamin D deficiency in South Asian developing world (Londhey, 2011).

Vitamin D deficiency is correlated to age and sex and exerts substantial negative effect in all age groups from infancy to old age. Sufficient information is available to demonstrate the decreased vitamin D level with progression of age which is exacerbated by sunshine avoidance for extended period of time (Holick, 1995). Though, serum 25(OH)D level decreases with increasing age however, response to a given dose of supplemental vitamin D_3 at serum 25(OH)D level, remained unaffected as compared to young population with similar skin and region (Harris and Dawson-Hughes, 2002). Another study reported decreased serum 25(OH)D level in elderly (75+ years) suggesting that cutaneous synthesis of 25(OH)D declines markedly with age resulting in vitamin D deficiency (Lips, 2001). Lower serum 25(OH)D level in old age may be ascribed to reduced ability of the skin to synthesize vitamin D on exposure to sunlight (van der Meer et al., 2011).

The differences in serum 25(OH)D levels among males and females in Indian sub-continent are primarily associated with clothing differences. Among Muslim communities in particular and non-Muslim societies at large, absence of veiling among adolescent girls and adult women is frowned on (Mishal, 2001).

A sizable body of literature confirmed the association of vitamin D deficiency with various anthropometric factors particularly body mass index (BMI). 25(OH)D concentrations have been shown to inversely associate with BMI and waist circumference in children (Alemzadeh et al., 2008; Rodrẽguez-Rodrẽguez et al., 2010; Smotkin-Tangorra et al., 2007). Other studies explained adiposity as a potential determinant of low vitamin D serostatus in school-age children with an effect on linear growth (Gilbert-Diamond et al., 2010).

An overwhelming amount of evidence exists to validate that environmental factors such as pollution, sunshine exposure habits, veil system among Muslims, inadequate nutritional supplementation, little or no vitamin D fortification of milk and milk products have magnified the prevalence of vitamin D in South Asian countries (Babu and Calvo, 2010; Calvo, 2004; Chris, 2006; Genuis et al., 2009). Vitamin D status of these populations is also correlated to rapid urbanization that has led to lower vitamin D reserves among urban populations in Asia as both men and women stay indoors (Heere et al., 2010; Manicourt and Devogelaer, 2008; Soontrapa et al., 2009).

Genetic factors influencing the vitamin D status of various populations encompass country of origin, behavior, cultural practices and skin pigmentation. Several studies indicated a transition in vitamin D levels among Asian migrants with relocation from the regions of low latitude to higher latitudes e.g Pakistani immigrants in Norway depicted lower serum vitamin D levels as compared with Vietnamese immigrants (Holvik et al., 2005). Many regional studies have confirmed the role of genetic factor in relation to vitamin D concentration around the globe.

Genetic basis of developing vitamin D deficiency involves genetic variation in cholesterol synthesis, hydroxylation, and vitamin D transport that normally results in increased risk of vitamin D insufficiency (Brock et al., 2007; Looker et al., 2002; Vieth et al., 2001).

Diagnosis and Treatment of Vitamin D Deficiency

The notion that a physician might diagnose hypovitaminosis D in the first instance, seems a little vague in South Asian perspective where symptomatic treatment is a commonplace and least attention is paid to the wide ranging diagnosis for a number of diseases particularly among rural folk. The patients of vitamin D deficiency are presented with the symptoms like muscular weakness, a feeling of heaviness in the legs and chronic musculoskeletal pain. These symptoms are not generally screened by the local physicians to investigate for low 25(OH)D levels. This situation is exacerbated by the socioeconomic status of the population as majority of the cases of osteomalacia and rickets are reported from low to middle income groups. The diagnosis for vitamin D deficiency is relatively expensive and the physicians and clinicians are generally reluctant to advise the test for serum 25(OH)D. The level of awareness about prevalence of vitamin D and its determinants among medical practitioners may also vary, depending upon several factors such as the level of expertise, the communities under treatment and the working location (rural/urban). Cannell et al., (2008) suggest sunlight exposure of 15 min of summer noonday one or two times a week to maintain 25(OH)D levels in healthy ranges however, special care is needed in avoiding sunburns, which are associated with malignant. Oral vitamin D treatment is relatively difficult than treatment for the reason that the requirement of the body for the amount of vitamin D varies with body weight, body fat, age, skin color, season, latitude and sunning habits.

However, timely advice by the health professionals to patients plays a critical role to prevent vitamin D deficiency. Holick (2005) suggested interpretation of serum 25(OH)D levels as a way to diagnose vitamin D deficiency at least twice in a year. Moreover, health professionals should focus upon vitamin D supplementation, increased exposure to sunlight, consumption of vitamin D fortified foods and a better dietary intake covering vitamin D rich foods to achieve desired 25(OH)D levels.

Vitamin D Intakes and Dietary Recommendations

Dietary intake of vitamin D significantly affects 25(OH)D levels in human body. Several studies have demonstrated an estimated intake of vitamin D to approximately 1 µg per day in Pakistan; seriously short of the daily requirement. Another study elucidated the association of calcium and vitamin D with bone density in rural communities in Pakistan suggesting calcium intake to 346 mg/d i.e. less than 50% of the recommended daily intake (Herm et al., 2005; Lowe et al., 2011). Similarly, dietary vitamin D intake has shown to be very low in India because of limited intake of vitamin D rich foods. Needs for vitamin D (50% and 90%) in Indian population are met by its production in the skin through UVB and the remainder is taken from the diet (Babu and Calvo, 2010; Lips, 2010). Requirements for vitamin D for maintaining a sufficient 25OHD level during winter has been reported to be >12.5 εg, however the requirements are much higher darkly pigmented, veiled, or sun protected persons i.e. >50 εg (Whiting et al., 2007). In Bangladesh, low frequency of intake of foods from animal source (other than fish) has been a potential cause among the mothers leading to low maternal-infant 25(OH)D(Roth et al., 2010a). Dietary vitamin D intake was found to be satisfactory in preschool children in Sri Lanka (Hettiarachchi and Liyanage, 2010).

Data for dietary intake of vitamin D are scant in South Asian developing countries. The author remained unsuccessful to catch on any specific study that focused on the comparison of recommended dietary allowance and the population intake of vitamin D in these regions. However, food consumption tables detailing the nutritive value of indigenous foods and 24 hrs.recall methods have been exploited to estimate the intake of several micronutrients in resource constrained countries of South Asia (Gopalan et al., 1996; Hakeem et al., 2002).

Strategies to Address Vitamin D Deficiency in South Asia

Success of food fortification is based upon certain determinants like the dietary habits of the population, approximate consumption of fortified products (Akhtar et al., 2011) and intakes of naturally occurring vitamin D in foods. Similarly, toxicological limits and any detrimental effect of fortificants on hematological body profile need special attention in such programs (Akhtar et al., 2011a,b). Supplementation bears some advantages over fortification for treating patients with chronic vitamin D deficiency and requires a substantial amount of personal compliance to maintain 25(OH)D levels in the body. Calvo et al. (2004) provide a plausible explanation of safety and efficacy for vitamin D fortification in the United States and Canada, suggesting to initiate more intervention studies for delineating potential approaches to control vitamin D deficiency among predisposed communities.

Dietary Diversification

Dietary diversification is a food based intervention strategy involving selection of foods that would simultaneously provide multiple micronutrients to combat nutritional deficiencies. Dietary diversification encompasses the assessment of dietary consumption, diversifying food production, improving food processing, preservation, storage and marketing. Evidently, this strategy seems to work well with nutritional education to enhance the total energy and micronutrient intake in developing countries (Tontisirin et al., 2002).

A most recent study reported 75ï 87.5 nmol 25(OH)D/L to be desirable to avoid vitamin D deficiency (Zittermann et al., 2012). To certain extent, dietary diversification seems to positively impact in meeting these needed levels of 25(OH)D. This strategy is sustainable and has the potential to enhance other micronutrientsô status among vulnerable populations. Dietary diversification has the advantage over other techniques in providing multiple nutrients rather a specific nutrient supplied through fortification or supplementation. For example, consuming vitamin A rich foods showed promising results in India to combat micronutrientsô deficiencies thus dietary diversification was encouraged as a potential approach to ensure nutrition security (Arlappa et al., 2011; Kapil and Tyagi, 2011).

Contrarily, the approach seemingly appeared to be less effective for certain limitations like a short range of foods containing naturally occurring vitamin D and their consumption is not as much regular. Many of the foods as natural sources e.g. oily fish, meat, dairy, egg yolk and mushrooms are not frequently available to the poorer populations for being more expensive and inaccessible. Therefore, mere dependence on natural foods to meet RDA for vitamin D seems to fail in controlling vitamin D deficiency.

Supplementation

Recent trends in the domain of nutritional sciences lead the scientists to recommend supplementation of vitamin D among children in South Asian regions (Casey et al., 2010; Lips, 2007). Vitamin D supplementation has shown to be a defense against vitamin D insufficiency and deficiency in South Asian countries. Several studies demonstrated supplementation of vitamin D to improve bone mineral density and attenuate the risk of falls and fractures in certain groups of people from western world (Ascherio et al., 2010; Pierrot-Deseilligny and Souberbielle, 2010). Notably high levels of vitamin D in elderly people were observed as a corollary on vitamin D supplementation with decreased synthesis of PTH, and better bone mineral density (BMD) of the lumbar spine and hip (Lips et al., 1988; Ooms et al., 1995).

Vitamin D status of the mothers in pregnancy determines vitamin D status of their infant, therefore normal maternal vitamin D level reduces the likelihood for resurgence of rickets among children (Dijkstra et al., 2007). Supplementation of vitamin D in India is not yet well structured and is not even widely practiced during pregnancy though the needs for vitamin D are higher during pregnancy. Dose of 400 IU as the dietary reference intake for vitamin D during pregnancy has been extensively argued and higher allowance (600 IU) has been recommended for vitamin D during pregnancy and lactation in India (Ooms et al., 1995; Onal et al., 2010).

There are no regular vitamin D supplementation programs currently existing in Pakistan. Patients suffering from vitamin D deficiency are treated by dispensing higher dose of vitamin D supplements namely ñIn drop Dò or Vitamin D shots (Calcitriol Injections). Similarly, there are hardly any data indicating a planned vitamin D supplementation program in Bangladesh and Sri Lanka.

Food Fortification

Vitamin D fortification of foods has long been practiced in the western world and promising results have been obtained for the efficacy of fortified foods e.g. 11 % of total vitamin D intake was noted from fortified foods in Ireland. Another success story for vitamin D fortification in Finland set an example for the world community to implement vitamin D fortification as a viable approach for controlling vitamin D deficiency (Hannon et al., 2007; Tylavsky et al., 2006). Fortification of specific foods with vitamin D is either mandatory or optional e.g. addition of vitamin D to margarine (Department of Health, 1998; Scientific Advisory Committee on Nutrition, 2007) in UK and juices and breakfast cereals (Calvo et al., 2004) in USA is mandatory. Practicing vitamin D fortification of a single staple like milk or dairy does not generally seem very practicable particularly in countries of developing world instead, a variety of foods needs to be considered for vitamin D fortification. Fortification of wheat flour considerably alleviated vitamin D deficiency in India and other countries in the region where consumption of pasteurized milk is not common (Babu and Calvo, 2010).

Mandatory fortification of vegetable oil is not appropriately practiced and many of the manufacturers of vegetable oil do not add reasonable levels of vitamin D, resulting in poorer supply of vitamin D to the consumers. There are no precise data available to suggest that the recommended levels of vitamin D are added to the vegetables oils in Pakistan and adjoining states. Moreover, little or no surveillance is existent to assess whether the fortification is even practiced. Wheat flour or cooking oil may be a better option for vitamin D fortification in Bangladesh (Misra et al., 2008). Since, the prevalence of vitamin D deficiency in Sri Lanka is relatively lower therefore, little or no work has been initiated in this regard. Paucity of literature to ascertain fortification of foods with vitamin D as an approach to control vitamin D deficiency remains to be a limitation.

Conclusions and future directions

It is virtually hard to predict the magnitude of vitamin D deficiency in low income South Asian developing countries in the absence of national level data. However, small studies representing higher magnitude of the prevalence of vitamin D deficiency in South Asia are not scant. A substantial faction of Indian, Pakistani, Bangladeshi and Sri Lankan populations were reported to suffer from vitamin D deficiency associating the deficiency with inadequate exposure to sunlight, skin pigmentation and insufficient consumption of dietary vitamin D. Poverty and illiteracy remain two underlying determinants to provoke vitamin D deficiency in these countries. The corollary of this widespread prevalence of hypovitaminosis D in these regions is rickets, osteomalacia, and osteoporosis and in some cases cancer and CVD. Amongst several risk factors for hypovitaminosis D, old age, latitude, winter season and skin pigmentation have been significant. There is a need to revitalize the whole health care systems in these culturally resembling poorer South Asian economies with drastic changes in cultural and dietary practices. Intervention programs in the form of supplementation and food fortification need to be launched at massive level in addition to the development of awareness to control overwhelming vitamin D deficiency in South Asia. Several limiting factors have been identified for precise estimation of vitamin D deficiency such as lack of interest among governments, lack of international reference materials, comparisons of adequacy across different countries and population groups, inadequacy of food consumption surveys, and education and advocacy. There is also a need to direct more studies in South Asia to evaluate the impact of vitamin D deficiency in relation to many chronic diseases and to assess the efficacy of supplementation and food fortification on the vitamin D status of South Asian populations. Certain strategies like enriching yeast by radiation in making bread, irradiating mushrooms and using 25(OH) D as meat tenderizer must be tested as potential strategies to curtail vitamin D deficiency in South Asia.

Conflict of interest

ACCEPTED MANUSCRIPT

There is no conflict of interest among authors and no funding is involved in the write up of this manuscript. The manuscript is the sole effort of author Saeed Akhtar.

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References

Agarwal, K. S., Mughal, M. Z., Upadhyay, P., Berry, J. L., Mawer, E. B., and Puliyel, J. M. (2002) The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi India. *Arch. Dis. Child.* **87:** 111-113.

Ahmed, T., Mahfuz, M., Ireen, S., Ahmed, A. M., Rahman, S., Islam, M. M., Alam, N., Hossain, M. I., Rahman, S. M., Ali, M. M., Choudhury, F. P., and Cravioto, A. (2012) Nutrition of Children and Women in Bangladesh: Trends and Directions for the Future. *J. Health Popul. Nutr.* **30**: 1-11.

Akhtar, S., Anjum, F. M., and Anjum, M. A. (2011). Micronutrient fortification of wheat flour: recent development and strategies. *Food Res. Intern.* **44**: 652-659.

Akhtar S, Anjum FM, Ur Rehman, Z., Sultan, M. T., Riaz, M., and Ahmed, A. (2011). Effect of Mineral Fortification on Plasma Biochemical Profile in Rats. *Biol. Trace Elem. Res.* **143**:1594-606.

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

Akhtar S, Anjum FM, Rehman, Z. U., Riaz, M., Arshad, M., Basit, A., and Ismail, T. (2011). Effect of zinc and iron fortification of feed on liver and thyroid function. *Biol. Trace Elem. Res.* **144**: 894-903.

Alemzadeh R, Kichler J, Babar G., and Calhoun, M. (2008). Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. *Metabolism* **57**: 183ï 91.

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

Anon. (2012). Dr. Duke's Phytochemical and Ethno botanical Databases Available at http://sun.arsgrin.gov:8080/npgspub/xsql/duke/plantdisp.xsql?taxon=606 Accessed on May 2012.

Arabi, A., El Rassi, R., and El-Hajj Fuleihan, G. (2010). Hypovitaminosis D in developing countriesð prevalence, risk factors and outcomes. *Nat. Rev. Endocrinol*. **6**: 550ï 561.

Arlappa, N., Balakrishna, N., and Laxmaiah, A. (2011). Prevalence of vitamin A deficiency and its determinants among the rural pre-school children of Madhya Pradesh, *India. Ann. Hum. Biol.* **38**: 131-136.

Arneil, G. C. (1975). Nutritional rickets in children in Glasgow. *Proc. Nutr. Soc.* **34**: 101ï 109.

Arya, V., Bhambri, R., Godbole, M. M., Mithal, A. (2004). Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. *Osteoporos. Int.* **15**: 56-61.

Ascherio, A., Munger, K. L., and Simon, K. C. (2010). Vitamin D and multiple sclerosis. *Lancetneurology* **9**: 599-612.

Atiq, M., Suria, A., Nizami, S. Q., and Ahmed, I. (1998). Maternal vitamin-D deficiency in Pakistan. *Acta. Obstet. Gynecol. Scand.* **77:** 970-3.

Atiq, M., Suria, A., Nizami, S. Q., Ahmed, I. (1998b). Vitamin D status of breastfed Pakistani infants. *Acta. Paediatr.* **87:** 737-40.

Babu, U. S., and Calvo, M. S. (2010). Modern India and the vitamin D dilemma: evidence for the need of a national food fortification program. *Mol. Nutr. Food Res.* **54**: 1134-47.

Bachelet, D., Barnes, P. W., Brown, D., Brown, M. (1991). Latitudinal and seasonal variation in calculated ultraviolet-B irradiance for rice-growing regions of Asia.*Photochem. Photobiol.* **54**: 411-22.

Balasubramanian, K., Rajeswari, J., Gulab, Govil, Y. C., Agarwal, A. K., Kumar, A., and Bhatia, V. (2003). Varying role of vitamin deficiency in the etiology of rickets in young children vs. adolescents in northern India. *J. Trop. Pediatr.* **49**: 201ï 6.

Bhatty, S. A., Shaikh, N. A., and Irfan, M. (2010). Vitamin D deficiency in fibromyalgia. *J. Pak. Med. Assoc.* **60:** 949-951.

Bischoff-Ferrari, H. A., Willett, W. C., Wong, J. B., Giovannucci, E., Dietrich, T., and Dawson-Hughes, B. (2005). Fracture prevention by vitamin D supplementation: a meta-analysis of randomized controlled trials. *J. Am. Med. Assoc.* **293**: 2257-2264.

Bouillon, R., Carmeliet, G., Daci, E., Segaert, S., and Verstuyf, A. (1998). Vitamin D metabolism and action. *Osteoporosis Int.* **8**: S13-9.

Brock, K., Cant, R., Clemson, L., Mason, R. S., and Fraser, D. R. (2007). Effects of diet and exercise on plasma vitamin D (25(OH) D) levels in Vietnamese immigrant elderly in Sydney. *Australia. J. Steroid. Biochem. Mol. Biol.* **103**: 786ï 792.

Brock, K., Wilkinson, M., Cook, R., Lee, S., and Bermingham, M. (2004). Associations with vitamin D deficiency in ñat riskò Australians. *J. Steroid Biochem. Mol. Biol.* **89–90:** 581ï 588.

Brooke, O. G., Brown, I. R., Bone, C. D., Carter, N. D., Cleeve, H. J., Maxwell, J. D., Robinson, V. P., and Winder, S. M. (1980). Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth**.** *Br. Med. J.* **15**: 751ï 754.

Calvo, M. S., Whiting, S. J., and Barton, C. N. (2004). Vitamin D fortification in the United States and Canada: current status and data needs. *Am. J. Clin. Nutr.* **80:** 1710Sï 1716S.

Cannell, J. J., Vieth, R., and Umhau, J. C. (2006). Epidemic influenza and vitamin D. *Epidemiol. Infect.* **134:** 1129ï 40.

Cannell, J. J., Hollis, B. W., Zasloff, M.,and Heaney R. P. (2008). Diagnosis and treatment of vitamin D deficiency. *Expert opin pharmaco*: **9(1):** 107-118.

Casey, C. F., Slawson, D. C., and Neal, L. R. (2010). Vitamin D Supplementation in Infants, Children, and Adolescents. *Am. Fam. Physician.* **81:** 745-748.

Cashman, K. D. (2002). Calcium intake, calcium bioavailability and bone health. *Br. J. Nutr.* **87**: S169-S177.

Chinoy, M. A., Javed, M. I., Khan, A., and Sadruddin, N. (2011). Alkaline phosphatase as a screening test for osteomalacia. *J. Ayub Med. Coll. Abbottabad.* **23:** 23-25.

Chris, M. (2006). From Seafood to Sunshine A New Understanding of Vitamin D Safety. *Wise Traditions,* 14-33.

Clemens, T. L., Adams, J. S., Henderson, S. L., and Holick, M. F. (1982). Increased skin pigmentation reduces the capacity of skin to synthesis vitamin D3. *Lancet* **1:** 74ï 76.

Cranney, A., Horsley, T., O'Donnell, S., Weiler, H., Puil, L., Ooi, D., Atkinson, S., Ward, L., Moher, D., Hanley, D., Fang, M., Yazdi, F., Garritty, C., Sampson, M., Barrowman, N., Tsertsvadze, A., and Mamaladze, V. (2007). Effectiveness and safety of vitamin D in relation to bone health. *Evid. Rep. Technol. Assess.* **158**: 1-235.

Craviari, T., Pettifor, J. M., and Thacher, T. D. (2008). Rickets: an overview and future directions, with special reference to Bangladesh. *J. Health Popul. Nutr.* **26:** 112-121.

Dawodu, A., and Wagner, C. L. (2007). Vitamin D Mother-child vitamin D deficiency: an international perspective. *Arch. Dis. Child.* **92**: 737-40.

deGruijl, F. R. (2011). Sufficient vitamin D from casual sun exposure? *Photochem. Photobiol.* **87:** 598ï 601.

Delvin, E. E., Salle, B. L., Glorieux, F. H., Adeleine, P., and David, L. S. (1986). Vitamin D supplementation during pregnancy: effect on neonatal calcium homeostasis. *J. Pediatr.* **109**: 328-34.

Department of Health. (1998). Nutrition and Bone Health: with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food and Nutrition Policy. London: The Stationery Office.

Diffey, B. L. (2010). Is casual exposure to summer sunlight effective at maintaining adequate vitamin D status**?** *Photodermatol. Photo*. **26:** 172ï 176.

Dijkstra, S. H., van Beek, A., Janssen, J. W., de Vleeschouwer, L. H., Huysman, W. A., and van den Akker, E. L. (2007). High prevalence of vitamin D deficiency in newborns of high-risk mothers. *Arch. Dis. Chld. Fetal. Neonatal Ed*. **92:** 750ï 753.

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

Fischer, P. R., Rahman, A., Cimma, J. P., Kyaw-Myint, T. O., Kabir, A. R., Talukder, K., Hassan, N., Manaster, B. J., Staab, D. B., Duxbury, J. M., Welch, R. M., Meisner, C. A., Haque, S., and Combs, G. F. Jr. (1999). Nutritional rickets without vitamin D deficiency in Bangladesh. *J. Trop. Pediatr.* **45:** 291-293.

Fleck, A. (1989). Latitude and ischaemic heart disease. *Lancet.* **1:** 613.

Genuis, S. J., Schwalfenberg, G. K., Hiltz, M. N., and Vaselenak, S. A. (2009). Vitamin D status of clinical practice populations at higher latitudes: analysis and application. *Int. J. Environ. Res. Public Health*. **6**: 151-173.

Gilbert-Diamond, D., Baylin, A., Mora-Plazas, M., Marin, C., Arsenault, J. E., Hughes, M. D., Willett, W. C., and Villamor, E. (2010). Vitamin D deficiency and anthropometric indicators of adiposity in school-age children: a prospective. *Am. J. Clin. Nutr*. **92(6)**: 1446-51.

Gopalan, C., Sastri, B. V. R., and Balasubramanyam, S. C. (1996). Food composition table. **In:** Nutritive value of Indian foods. pp. 92-94. India: National Institute of Nutrition (ICMR) Hyderabad.

Goswami, D., Marwaha, R. K., Tandon, N., and Kochupillai, N. (2000). Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am. J. Clin. Nutr.* **72**: 472-475.

Goswami, R., Marwaha, R. K., Gupta, N., Tandon, N., Sreenivas, V., Tomar, N., Ray, D., Kanwar, R., and Agarwal, R. (2009). Prevalence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey. *Br. J. Nutr.* **102:** 382ï 386.

Grant, W. B., and Holick, M. F. (2005). Benefits and requirements of vitamin D for optimal health: a review. *Altern. Med. Rev.* **10**: 94-111.

Grant, W. B. (2003). Ecologic studies of solar UV-B radiation and cancer mortality rates. *Recent Results Cancer Res.* **164**: 371-377.

Grimes, D. S., Hindle, E., and Dyer, T. (1996). Sunlight, cholesterol and coronary heart disease. *QJM.* **89**: 579-589.

Haider, N., Nagi, A. G., and Khan, K. M. A. (2010). Frequency of nutritional rickets in children admitted with severe pneumonia. J. Pak. Med. Assoc. **60**: 729-32.

Hakeem, R., Thomas, J., and Badruddin, S. H. (2002). Food Habits and Nutrient Density of Diets of Pakistani Children Living in Different Urban and Rural Settings. *J. Health Popul. Nutr.* **20:** 255-263.

Hameed, A., Saleem, A., **Rehman, S. U., Aurakzai, A. A., and Gandapoor, A. J.** (1998). A study of rickets - morbidity and aetiology of a low profile disorder. *JPMI* **12:** 14-21.

Hannon, E. M., Kiely, M., and Flynn, A. (2007). The impact of voluntary fortification of foods on micronutrient intakes in Irish adults. *Br. J. Nutr.* **97:** 1177-1186.

Harinarayan, C. V. (2005). Prevalence of vitamin D insufficiency in postmenopausal south Indian women. *Osteoporos. Int*. **16**: 397-402.

Harinarayan, C. V., Ramalakshmi, T., Prasad, U. V., Sudhakar, D., Srinivasarao, P. V., Sarma, K. V., and Kumar, E. G. (2007). High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am. J. Clin. Nutr.* **85:** 1062-7.

Harinarayan, C. V., Sachan, A., Reddy, P. A., Satish, K. M., Prasad, U. V., and Srivani, P. (2011). Vitamin D status and bone mineral density in women of reproductive and postmenopausal age groups: a cross-sectional study from south India. *J. Assoc. Physicians India.* **59**: 698-704.

Harinarayan, C. V., and Joshi, S. R. (2009). Vitamin D status in India-its implications and remedial measures. *J. Assoc. Physicians India.* **57**: 40-8.

Harris, S. S., and Dawson-Hughes, B. (2002). Plasma vitamin D and 25OHD responses of young and old men to supplementation with vitamin D3. *J. Am. Coll. Nutr.* **21**: 357ï 362.

Heere, C., Skeaff, C. M., and Waqatakirewa, L. (2010). Serum 25-hydroxyvitamin D concentration of Indigenous-Fijian and Fijian-Indian women. *Asia Pac. J. Clin. Nutr.* **19**: 43-48.

Herm, F. B., Killguss, H., and Stewart, A. G. (2005). Osteomalacia in Hazara district, Pakistan. *Trop. Doct*. **35**: 8-10.

Hettiarachchi, M., and Liyanage, C. (2010). Coexisting micronutrient deficiencies among Sri Lankan pre-school children: a community-based study. *Matern. Child Nutr.* **8:** 259-66.

Hettiarachchi, M., Lekamwasam, S., and Liyanage, C. (2011). Bone mineral density and nutritional status of healthy Sri Lankan preschool children. *Int. J. Endocriol. Metab.* **9:** 317-22.

Hettiarachchi, M., and Liyanage, C. (2010). Dietary macro- and micro-nutrient intake among a cohort of pre-school children from Southern Sri Lanka. *Ceylon. Med. J.* **55:** 47-52.

Holick, M. F., and Chen, T. C. (2008). Vitamin D deficiency: a worldwide problem with health consequences. *Am. J. Clin. Nutr.* **87**: 1080S-1086S.

Holick, M. F. (1995). Environmental factors that influence the cutaneous production of vitamin D. *Am. J. Clin. Nutr.* **61**: 638S-645S.

Holick, M. F. (2005). The vitamin D epidemic and its health consequences. *J. Nutr*. **135:** S2739-48.

Holick, M. F., Biancuzzo, R. M., Chen, T. C., Klein, E. K., Young, A., Bibuld, D., Reitz, R., Salameh, W., Ameri, A., and Tannenbaum, A. D. (2007). Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D. *J. Clin. Endocrinol. Metab.* **93**: 677-681.

Holick, M. F., Binkley, N. C., Bischoff-Ferrari, H. A., Gordon, C. M., Hanley, D. A., Heaney, R. P., Murad, M. H., Weaver, C. M. Endocrine Society (2011). Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J. Clin. Endocrinol. Metab.* **96**: 1911-30.

Holick, M. F., Maclaughlin, J. A., and Doppelt, S. H. (1981). Regulation of cutaneous pre-vitamin D3 photosynthesis in manskin pigment is not an essential regulator. *Science* **211**: 590ï 593.

Holick, M. F. (2006). High prevalence of vitamin D inadequacy and implications for health. *Mayo. Clin. Proc*. **81:** 353-73.

Holvik, K., Meyer, H. E., Haug, E., and Brunvand, L. (2005). Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway: the Oslo Immigrant Health Study. *Eur. J. Clin. Nutr.* **59**: 57ï 63.

Hossain, N., Khanani, R., Hussain-Kanani, F., Shah, T., Arif, S., and Pal, L. (2011). High prevalence of vitamin D deficiency in Pakistani mothers and their newborns. *Int. J. Gynaecol. Obstet.* **112**: 229-33.

Houghton, L. A., and Vieth, R. (2006). The case against ergocalciferol (vitamin D2) as a vitamin supplement. *Am. J. Clin. Nutr.* **84**: 694-7.

Imtiaz, S., Siddiqui, N., Raza, S. A., Loya, A., and Muhammad, A. (2012). Vitamin D deficiency in newly diagnosed breast cancer patients. *Indian J. Endocrinol. Metab*. **16:** 409-13.

Islam, M. Z., Akhtaruzzaman, M., and Lamberg-Allardt, C. (2006). Hypovitaminosis D is common in both veiled and non-veiled Bangladeshi women. *Asia Pac. J. Clin. Nutr.* **15**: 81ï 87.

Islam, M. Z., Lamberg-Allardt, C., Kärkkäinen, M., Outila, T., Salamatullah, Q., and Shamim, A. A. (2002). Vitamin D deficiency: a concern in premenopausal Bangladeshi women of two socio-economic groups in rural and urban region. *Eur. J. Clin. Nutr.* **56**: 51ï 56.

Virtanen, J. K., Nurmi, T., Voutilainen, S., Mursu, J., and Tuomainen, T. P. (2011). Association of serum 25-hydroxyvitamin D with the risk of death in a general older population in Finland. *Eur. J. Nutr.* **50**: 305-312.

Kabir, M. L., Rahman, M., Talukder, K., Rahman, A., Hossain, Q., Mostafa, G., Mannan, M. A., Kumar, S., and Chowdhury, A. T. (2004). Rickets among children of a coastal area of Bangladesh. *Mymensingh Med. J.* **13:** 53-8.

Kapil, U., and Tyagi, M. (2011). Scientific rationale for targeted vitamin A supplementation to children in India. *Indian J. Community Health.* **23**: 1-3.

Karim, F., Chowdhury, A. M., and Gani, M. S. (2003). Rapid assessment of the prevalence of lower limb clinical rickets in Bangladesh. *Pub. Health*. **117**: 135-44.

Karim, S. A., Nusrat, U., and Aziz, S. (2011). Vitamin D deficiency in pregnant women and their newborns as seen at a tertiary-care center in Karachi, Pakistan. *Int. J. Gynecol. Obstet.* **112**: 59-62.

Khadilkar, A. V. (2010). Vitamin D deficiency in Indian Adolescents. *Indian Pediatrics.* **47**: 756-757.

Khattak, A. A., Rehman, G., Shah, F. U., and Khan, M. K. (2004). Study of rickets in admitted patients at LRH, Peshawar. *JPMI.* **18**: 52-58.

Kiely, M., and Black, J. L. (2012). Dietary strategies to maintain adequacy of circulating 25-Hydroxyvitamin D concentrations. *Scand. J. Clin. Lab. Invest.* **72**: 14-23.

Kimlin, M. G., William, J. O., and Michael, R. M. (2007). Location and Vitamin D synthesis: Is the hypothesis validated by geophysical data? *J. Photochem. Photobiol. B–Biol.* **86:** 234ï 239.

Koyyalamudi, S. R., Jeong, S. C., and Song, C. H., (2009). Vitamin D2 formation and bioavailability from *Agaricusbisporus* button mushrooms treated with ultraviolet irradiation. *J. Agric. Food Chem.* **57:** 3351ï 5.

Lee, J. H., OôKeefe, J. H., Bell, D., Hensrud, D. D., and Holick, M. F. (2008). Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? *J. Am. Coll. Cardiol.* **52**: 1949-1956.

Lerch, C., and Meissner, T. (2007). Interventions for the prevention of nutritional rickets in term born children. *Cochrane DB. Syst. Rev.* **4**. Art. No.: CD006164. DOI: 10.1002/14651858.CD006164.pub2.

Lips, P. (1998). Does calcium intake change vitamin D requirements? **In:** Nutritional aspects of osteoporosis, pp. 262-267. Burckhardt, P., Dawson, H. B., and Heaney, R. P., Eds., Springer-Verlag, New York.

Lips, P. (2001). Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr. Rev.* **22**: 477-501.

Lips, P., Chapuy, M. C., Dawson-Hughes, B., Polis, H. A., and Holick, M. F. (1999). An international comparison of serum 25-hydroxyvitamin D measurements. *Osteoporos Int.* **9**: 394 -397.

Lips, P., Wiersinga, A., van Ginkel, F. C., Jongen, M. J., Netelenbos, J. C., Hackeng, W. H., Delmas, P. D., and van der Vijgh, W. J. (1988). The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J. Clin. Endocrinol. Metab.* **67**: 644ï 650.

Lips, P. (2010). Worldwide status of vitamin D nutrition*. J. Steroid Biochem. Mol. Biol*. **121**: 297-300.

Lips, P. J. (2007). Vitamin D status and nutrition in Europe and Asia. *Steroid Biochem. Mol. Biol*. **103**: 620-5.

Londhey, V. (2011). Vitamin D deficiency: Indian scenario. *JAPI.* **59**: 695-696.

Looker, A. C., Dawson-Hughes, B., Calvo, M. S., Gunter, E. W., Sahyoun, N. R. (2002). Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone,* **30**: 771ï 777.

Lowe, N. M., Ellahi, B., Bano, Q., Bangash, S. A., Mitra, S. R., and Zaman, M. (2011). Dietary calcium intake, vitamin D status, and bone health in postmenopausal women in rural. Pakistan *J. Health Popul. Nutr*. **29:** 465-70.

Malhotra, N., Mithal, A., and Gupta, S. (2008). Effect of vitamin D supplementation on bone health parameters of healthy young Indian women. *Osteoporos. Int.* **19:** S29ï S207.

Manicourt, D. H., and Devogelaer, J. P. (2008). Urban tropospheric ozone increases the prevalence of vitamin D deficiency among Belgian postmenopausal women with outdoor activities during summer. *J. Clin. Endocrinol. Metab*. **93**: 893-3899.

Mansoor, S., Habib, A., Ghani, F., Fatmi, Z., Badruddin, S., Manzoor, S., Siddiqui, I., and Jabbar, A. (2010). Prevalence and significance of vitamin D deficiency and insufficiency among apparently healthy adults. *Clin. Biochem.* **43**: 1431-5.

Marwaha, R. K., and Sripathy, G. (2008). Vitamin D & bone mineral density of healthy school children in northern India. *Indian J. Med. Res.* **127**: 239-244.

Goswami, R., Gupta, N., Goswami, D., Marwaha, R. K., Tandon, N., and Kochupillai, N. (2005). Prevalence and significance of low 25- hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am. J. Clin. Nutr*. **82**: 477-82.

Marwaha, R. K., Tandon, N., Garg, M. K., Kanwar, R., Narang, A., Sastry, A., Saberwal, A., and Bandra, K. (2011). Vitamin D status in healthy Indians aged 50 years and above. *J. Assoc. Physicians India,* **59**: 703-707.

Marya, R. K., Saini, A. S., Rathee, S., Arora, S. R. (1980). Osteomalacia in Hindu population of Haryana. *Indian J. Med. Res.* **3:** 756ï 60.

Marya, R. K., Saini, A. S., Rathee, S., Arora, S. R. (1981). Osteomalacia in Hindu population of Haryana. *Indian J. Med. Res.* **73:** 756-60.

McGreevy, C., and Williams, D. (2011). New insights about vitamin D and cardiovascular disease: A narrative review. *Ann. Intern. Med.* **155**: 820ï 6.

Meyer, H. E., Falch, J. A., Sogaard, A. J., and Hauq, E. (2004). Vitamin D deficiency and secondary hyperparathyroidism and the association with bone mineral density in persons with Pakistani and Norwegian background living in Oslo, Norway: The Oslo Health Study. *Bone*, **35:** 412-17.

Meyer, H. E., Holvik, K., Lofthus, C. M., and Tennakoon, S. L. J. (2008). Vitamin D status in Sri Lankans living in Sri Lanka and Norway. *Br. J. Nutr.* **99:** 941-4.

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

Misra, M., Pacaud, D., Petryk, A., Collett-Solberg, P. F., Kappy, M., and Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. (2008). Vitamin D deficiency in children and its management: review of current knowledge and recommendations. *Pediatrics,* **122**: 398-417.

Mithal, A., Wahl, D. A., Bonjour, J. P., Burckhardt, P., Dawson-Hughes, B., Eisman, J. A., El-Hajj Fuleihan, G., Josse, R. G., Lips, P., Morales-Torres, J., and IOF Committee of Scientific Advisors (CSA) Nutrition Working Group. (2009). Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos. Int.* **20:** 1807-1820.

Mizoue, T. (2004). Ecological study of solar radiation and cancer mortality in Japan. *Health Phys.* **87**: 532-538.

Nair, R., and Maseeh, A. (2012). Vitamin D: The ñsunshineò vitamin. *J. Pharmacol. Pharmacother.* **3**: 118.

Nieves, J. W. (2005). Osteoporosis: the role of micronutrients. *Am. J. Clin. Nutr.* **81:** 1232S-1239S.

Nnoaham, K. E., and Clarke, A. (2008). Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis. *Intern. J. Epidemiol.* **37**: 113-9.

NNS (National Nutrition Survey Report) (2011) Government of Pakistan-Islamabad.

Onal, H., Adal, E., and Alpaslan, S. (2010). Is daily 400 IU of vitamin D supplementation appropriate for every country? : a cross-sectional study. *Eur. J. Nutr.* **49**: 395-400.

Ooms, M. E., Roos, J. C., Bezemer, P. D., van der Vijgh, W. J., Bouter, L. M., and Lips, P. (1995). Prevention of bone loss by vitamin D supplementation in elderly women: a randomized double blind trial. *J. Clin. Endocrinol. Metab.* **80:** 1052-1058.

Paul, G., Brehm, J. M., Alcorn, J. F., Holguín, F., Aujla, S. J., and Celedón, J. C. (2012). Vitamin D and asthma. *Am. J. Respir. Crit. Care Med.* **185**: 124-32.

Peterlik, M., Boonen, S., and Heide, S. (2009). Vitamin D and calcium insufficiency-related chronic diseases: an emerging world-wide public health problem. *Int. J. Environ. Res. Public Health.* **6**: 2585-2607.

Pettifor, J. M. (2008). Vitamin D &/or calcium deficiency rickets in infants & children; a global perspective. *Indian J. Med. Res.* **127**: 245-249.

Pettifor, J. M. (2004). Nutritional rickets: deficiency of vitamin D, calcium, or both? *Am. J. Clin. Nutr.* **80:** 1725S-9S.

Pierrot-Deseilligny, C., and Souberbielle, J. C. (2010). Is hypovitaminosis D one of the environmental risk factors for multiple sclerosis? *Brain: J. Neurol.* **133**: 1869-88.

Pittas, A. G., Chung, M., Trikalinos, T., Mitri, J., Brendel, M., Patel, K., Lichtenstein, A. H., Lau, J., and Balk, E. M. (2010). Systematic review: Vitamin D and cardiometabolic outcomes. *Ann. Intern. Med.* **152:** 307ï 14.

Pittas, A. G., Harris, S. S., Stark, P. C., and Dawson - Hughes, B. (2007). The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in non-diabetic adults. *Diabetes Care,* **30**: 980ï 986.

Prentice, A. (2008). Vitamin D deficiency: a global perspective. *Nutr. Rev.* **66:** S153ï S164.

Puri, S., Marwaha, R. K., Agarwal, N., Tandon, N., Agarwal, R., Grewal, K., Reddy, D. H., and Singh, S. (2008). Vitamin D status of apparently healthy schoolgirls from two different socioeconomic strata in Delhi: relation to nutrition and lifestyle. *Br. J. Nutr.* **99**: 876-882.

Purvis, R. J., Barrie, W. J., MacKay, G. S., Wilkinson, E. M., Cockburn, F., and Belton, N. R. (1973). Enamel hypoplasia of the teeth associated with neonatal tetany: a manifestation of maternal vitamin D deficiency. *Lancet.* **2**: 811-4.

Qamar, S., Akbani, S., Shamim, S., Khan, G. (2011). Vitamin D levels in children with growing pains. *J. Coll. Physician Surg. Pak.* **21:** 284-287.

Rathi, N., and Rathi, A. (2011). Vitamin D and child health in the 21st century. *Indian Pediatr*. **48:** 619-625.

Reeder, A. I., Janet, A. J., and Andrew, R. G. (2012). Prescribing sunshine: a national, cross-sectional survey of 1,089 New Zealand general practitioners regarding their sun exposure and vitamin D perceptions, and advice provided to patients. *BMC Family Practice,* **13**: 85.

Rizzoli, R., and Bonjour, J. (2004). Dietary protein and bone health. *J. Bone Miner. Res.* **19:** 527.

Rodriguez-Rodriguez, E., Navia-Lomban, B., Lopez-Sobaler, A. M., and Ortega, R. M. (2010) Associations between abdominal fat and body mass index on vitamin D status in a group of Spanish schoolchildren. *Eur. J. Clin. Nutr.* **64**: 461-67.

Rostand, S. G. (1979). Ultraviolet light may contribute to geographic and racial blood pressure differences. *Hypertension,* **30:** 150-156.

Roth, D. E., Shah, M. R., Black, R. E., and Baqul, A. H. (2010a). Vitamin D status of infants in northeastern rural Bangladesh: preliminary observations and a review of potential determinants. *J. Health Popul. Nutr*. **28:** 458-69.

Roth, D. E., Shah, R., Black, R. E., and Baqul, A. H. (2010). Vitamin D status and acute lower respiratory infection in early childhood in Sylhet, Bangladesh*. Acta Paediatr.* **99:** 389-393.

Sachan, A., Renu, G., Vinita, D., Agarwal, A., Awasthi, P. K., and Bhatia, V. (2005). High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am. J. Clin. Nutr.* **81**: 1060ï 4.

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

Scientific Advisory Committee on Nutrition. (2007). Update on Vitamin D. London: The Stationery Office.

Shaheen, S., Noor, S. S., and Barakzai, Q. (2012). Serum alkaline phosphatase screening for vitamin D deficiency states. *J. Coll. Physicians Surg. Pak*. **22**: 424-7.

Shivane, V. K., Sarathi, V., Bandgar, T., Menon, P., and Shah, N. S. (2011). High prevalence of hypovitaminosis D in young healthy adults from the western part of India. *Postgrad. Med. J.* **87**: 514-8.

Smotkin-Tangorra, M., Purushothaman, R., and Gupta, A. (2007). Prevalence of vitamin D insufficiency in obese children and adolescents. *J. Pediatr. Endocrinol. Metab.* **20**: 817ï 23.

Soontrapa, S., and Chailurkit, L. O. (2009). Hypovitaminosis D in Thailand. *J. Med. Assoc. Thailand*, **92:** S26-S29.

Talaei, A., Yadegari, N., Rafee, M., Rezvanfar, M. R., and Moini, A. (2012). Prevalence and cut-off point of vitamin D deficiency among secondary students of Arak, Iran in 2010; *Indian J. Endocr. Metab.* **16**: 786-790.

Tare, M., Emmett, S. J., Coleman, H. A., Skordilis, C., Eyles, D. W., Morley, R., and Parkington, H. C. (2011). Vitamin D insufficiency is associated with impaired vascular endothelial and smooth muscle function and hypertension in young rats. *J. Physiol.* **589:** 4777-4786.

Tenta, R., Moschonis, G., and Koutsilieris, M. (2011). Calcium and vitamin D supplementation through fortified dairy products counter balances seasonal variations of bone metabolism indices: the Postmenopausal Health Study. *Eur. J. Nutr.* **50:** 341-349.

Teotia, S. P. S., and Teotia, M. (2008). Nutritional bone disease in Indian population. *Indian J. Med. Res*. **127**: 219- 28.

Tontisirin, K., Nantel, G., and Bhattacharjee, L. (2002). Food-based strategies to meet the challenges of micronutrient malnutrition in the developing world. **In:** Proceedings-Nutrition Society of London, pp. 243-250. CABI Publishing: 1999.

Tylavsky, F. A., Cheng, S., and Lyytikainen, A. (2006). Strategies to improve vitamin D status in northern European children: exploring the merits of vitamin D fortification and supplementation. *J. Nutr.* **136**: 1130-1134.

Vaishnava, H. P., and Rizvi, S. N. A. (1967). Osteomalacia in northern India. *Br. Med. J.* **1**:112

van der Meer, I. M., Boeke, A. J., Lips, P., Grootjans-Geerts, I., Wuister, J. D., Deville, W.L., Wielders, J. P., Bouter, L. M., and Middelkoop, B. J. (2008). Fatty fish and supplements are the greatest modifiable contributors to the serum 25-hydroxyvitamin D concentration in a multiethnic population. *Clin. Endocrinol.* **68:** 466ï 472.

van der Meer, I. M., Karamali, N. S., Boeke, A. J., Lips, P., Middelkoop, B. J., Verhoeven, I., Wuister, J. D. (2006). High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am. J. Clin. Nutr.* **84**: 350ï 353.

van der Meer, I. M., Middelkoop, B. J. C., Boeke, A. J. P., and Lips, P. (2011) Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and sub-Sahara African populations in Europe and their countries of origin: an overview. *Osteoporos. Int.* **22**: 1009ï 1021.

Vieth, R., Bischoff-Ferrari, H., Boucher, B. J., Dawson-Hughes, B., Garland, C. F., Heaney, R. P., Holick, M. F., Hollis, B. W., Lamberg-Allardt, C., McGrath, J. J., Norman, A. W., Scragg, R., Whiting, S. J., Willett, W. C., and Zittermann, A. (2007). The urgent need to recommend an intake of vitamin D that is effective. *Am. J. Clin. Nutr.* **85**: 649ï 650.

Vieth, R., Cole, D. E., Hawker, G. A., Trang, H. M., and Rubin, L. A. (2001). Wintertime vitamin D insufficiency is common in young Canadian women, and their vitamin D intake does not prevent it. *Eur. J. Clin. Nutr.* **55:** 1091ï 1097.

Virmani, A. (2006). Vitamin D Deficiency. *Apollo Medicine,* **3**: 202-205.

von Hurst, P. R., Welma, S., and Jane, C. (2009). Vitamin D status and attitudes towards sun exposure in South Asian women living in Auckland, New Zealand. *Pub. Health Nutr*. **13**: 531ï 536.

Whiting, S. J., Green, T. J., and Calvo, M. S. (2007). Vitamin D intakes in North America and Asia-Pacific countries are not sufficient to prevent vitamin D insufficiency. *J. Steroid Biochem. Mol. Biol*. **103**: 626-630.

Wilson, D. C. (1931). The incidence of osteomalacia and late rickets in northern India. *Lancet*, **218**: 10-2.

Wolf, G. (2004). The Discovery of Vitamin D: The Contribution of Adolf Windaus. *J. Nutr*. **134**: 1299ï 1302.

Zittermann, A., Simona, I., and Stefan, P. (2012). Vitamin D deficiency and mortality risk in the general population: a meta-analysis of prospective cohort studies. *Am. J. Clin. Nutr.* **95**: 91-100.

Zittermann, A., Gummert, J. F., and Borgermann, J. (2009). Vitamin D deficiency and mortality. *Curr. Opin. Clin. Nutr. Metab. Care,* **12**: 634ï 9.

Table1.Vitamin D deficiency (%) based on 25(OH)D levels among pregnant and non-pregnant mothers in Pakistan

	Total	Residence		Province / Region						
		Urban	Rural	Punjab	Sindh	KPK	Baluchistan	FATA	AJK	Gilgit
Vitamin D Deficiency ï Non- Pregnant Mothers										
Severe Deficiency (<20nmol/L)	25.3	46.3	18.4	25.1	30.7	12.7	21.1	7.6	25.4	21
Deficiency (20-50 nmol/L)	40.9	30.5	44.4	40.9	42.4	32.1	36	46.9	48.2	66.1
Desirable (>50-75nmol/L)	18.8	11.2	21.4	17.5	17	34.7	25.5	30.6	21.5	9.1
Sufficient (>75nmol/L)	14.9	12.1	15.8	16.5	10	20.5	17.4	15	4.9	3.8
N	5402	1965	3437	3023	1154	290	363	32	334	206
Vitamin D Deficiency - Pregnant Mothers										
Severe Deficiency (<20nmol/L)	26.5	50.7	20.2	29.3	22.8	12.7	22.5	0	15	68.9

Deficiency (20-50 nmol/L)	42	27.7	45.7	41.9	44.7		26.5	26.8	0	60.2	22.5
Desirable (>50-75nmol/L)	17.6	7.9	20.1	16.4	17.1		38.3	28.3	0	10.3	4.3
Sufficient (>75nmol/L)	13.9	13.7	13.9	12.3	15.4		22.5	22.4	0	14.5	4.3
N	699	222	477	400	189		20	41	0	39	10

Derived from; National Nutrition Survey Report (2011) Govt. of Pakistan (NNS)

N= No. of participants

Table 2. Summary of some of the major recent studies on prevalence of vitamin D in India, Pakistan, Bangladesh and Sri Lanka

Study	Ref	Participants	Life stage	Location	No.	Prevalence of vitamin D deficiency
Agarwal et al, (2002)		Children	9-24 months	Delhi/ India	34	Comparison of two congested areas in India were studies with reference to environmental pollution. The mean total serum 25(OH)D concentration of children in highly polluted area was significantly lower than those of, living in relatively less polluted area, suggesting atmospheric pollution as a t risk of developing vitamin D deficiency rickets
Arya et al, (2004)		Healthy volunteers	34.2 (±6.7) years	Lucknow/ India	92	Out of total study population, only 31 (33.7%) subjects were shown to have sufficient vitamin D [serum 25(OH)D concentration above 15 ng/ml]. Nineteen (20.6%) subjects showed severe vitamin D deficiency and 25 (27.2%) had moderate vitamin D deficiency.

Harinarayan et al (2007)	Health and rural urban subject	---	South India	1148	The dietary phytate-to-calcium ratio was higher in rural subjects. Low dietary calcium intake and 25(OH)D conc. were associated with bone mineral homeostasis.
Harinarayan et al, (2011)	Post-menopausal women	----	South India	191	Osteoporosis was seen at hip (15% and 28%). Vitamin D deficiency was defined as 25(OH)D deficiency (< 50nmol/L), insufficiency (50-75 nmol/L).
Hettiarachchi & Liyanage (2010)	Children	3-5 years	Sri Lanka /Galle	248	26% and 25% of male and female were affected by vitamin D deficiency [(25(OH)D < 35nmol/L)] respectively.
Hettiarachchi et al, (2011)	Preschool children	3ï 5 years	Southern Sri Lanka	105	This study indicated higher bone area in the spine among boys as compared to girls . Corelation was developed as one unit change in body weight (1 kg) or serum calcium level (1 mmol/L) was shown to associate with a change in spine BMD of 0.051 g/cm2 or 0.016 g/cm^2, respectively.
Imtiaz et al, (2012)	Breast cancer patients		Lahore /Pakistan	90	95.6% (86) of the subjects examined showed vitamin D deficiency. No significant

					associations with serum levels of vitamin D with tumor characteristics could be established.
Islam *et al. 2002*	Females	16 ï 40 Years	Bangladesh Dhaka/ Nandail	197	12 -17% of the study population in suffered from vitamin D deficiency [25 (OH)D < 25nmol/L]
Kabir et al (2004)	Children	1-15 years	Chakaria /Bangladesh	900	Out of the total subjects under study only 8 (0.9%) children had 'confirmed rickets' (positive physical features, raised ALP and positive radiology).
Marwaha et al, (2011)	Healthy subjects	> 50 years	Delhi/ India	1346	Around 91.2% of the study population manifested vitamin D deficiency [(25(OH) D < 50nmol/L)], 6.8% showed vitamin D insufficiency, [(25(OH)D < 75nmol/L)].
Meyer et al, (2008)	Adults	30-60 years	Kandy/ Sri Lanka	196	Comparison showed Sri Lankans living in Norway had lower 25(OH)D (31·5 nmol/L) as compared with those living in Sri Lanka (54·2 nmol/L).
Peterlik et al.(2009)	General population	----	Global	Varied	30ï 80% population from Europe, North America, South-East Asia and South Pacific was distressed with

					vitamin D deficiency, cut off values for 25(OH)D defined for each country
Puri *et al. 2008*	Female	6-18 years	India (Delhi)	3127	Of the total population studies,90·8% of girls had hypovitaminosis D [(25(OH)D < 50nmol/L)].
Roth et al, (2010)	Children	1-18 months	Rural Bangladesh	50	25(OH) D was significantly lower among acute lower respiratory infection (ALRI) cases than controls. The study concluded that VDD was associated with early childhood ALRI.
Roth et al, (2010 a)	Infants	1-6 months	Rural Sylhet/ Bangladesh	29	28% of infants had 25(OH)D < 25 nmol/L, 59% had 25(OH)D < 40 nmol/L in a pneumonia case-control study . However, all subjects under study were below 80 nmol/L.
Sachan et al, (2005)	Pregnant Women	24.0 (±4.11) years	Lucknow/ India	207	Maternal serum 25(OH)D_10 ng/mL was found in 88women (42.5%), whereas 138 women (66.7%) had values ~15 ng/mL.
Sahibzada et al (2004)	Women of reproductive age	23 years	Kohistan/Pakistan		This study reported 12-16% of healthy women and 33% of pregnant women to

					have biochemical abnormalities of serum calcium, phosphorus, and alkaline phosphatase, that were corrected with subsequent administration of vitamin D.
Shivane et al (2011)	Healthy volunteers	25-35years	Western India	1137	The results of this study indicated 70 % of the study population to have hypovitaminosis D (25(OH)D <20 ng/ml) with a slightly higher prevalence in women (76%).

Table 3. Prevalence and predictors of hypovitaminosis D in India, Pakistan and Bangladesh

Region /Country	Reference	City (latitude)	Age Group	Prevalence %	Cut-off value (nmol/L)	Predictors of Vitamin D level
India	Marwaha *et al*. (2005)	New Delhi (28.0° N)	Children 10ï 18 years	27ï 42.3	<22.5	SES, sex
	Sachan *et al.* (2005)	Lucknow (26.8° N)	Pregnant women	42	<25.0	calcium intake
Pakistan	Atiq *et al.* (1998)	Karachi (24.5° N)	Mothers and infants	55 (infants) 45 (mothers)	<25.0	Age, season, maternal education, maternal vitamin D level
Bangladesh	Islam *et al*. (2002)	Dhaka (23.4° N) Nandail (15.2° N)	Adult women 16ï 40 yr	12ï 17 38ï 50	<25.0 <37.5	SES, dress style parity, level of sun exposure
	Islam *et al*. (2006)	Dhaka (23.4° N)	Women 18ï 60 yr	78ï 83	<40.0	

SES=Socio economic Status

Derived From; Arabi et al (2010)