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A Review

Prevalence of vitamin D deficiency in pregnancy among Indian population: A systematic review

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■ **ABSTRACT :** The prevalence of vitamin D deficiency (VDD) is increasing worldwide among all age groups including pregnant females. In our manuscript, we aim to review the existing literature to assess the prevalence of VDD among pregnant females in Indian population and to identify risk factors associated with it. We performed a systematic literature search of PubMed upto October 2018 for relevant articles. We found that prevalence ranged from 56 per cent to 96 per cent. Most of the studies found positive correlation between sun exposure and serum vitamin D level. Four studies found higher prevalence of VDD during winters while one study found higher prevalence during summers. Prevalence was similar among various religions. One study reported lower prevalence among non-vegetarians. Two studies showed no association of daily calcium intake and maternal serum vitamin D level while one study found low intake is associated with low vitamin D level. We conclude that even after adequate sunlight availability in India the prevalence of VDD is very high but further studies are required on vitamin D supplementation to understand its effect on prevention of VDD.

■ **KEY WORDS:** Vitamin D deficiency, Pregnant females, Prevalence, Hypovitaminosis, Risk factors

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The prevalence of vitamin D deficiency (VDD) is increasing worldwide among all age groups including pregnant females (Holick *et al.,* 2011). Vitamin D plays important role in bone formation. It is required for adequate absorption of calcium. Sunlight is one of the most important natural source of vitamin D with food and supplements also playing an important role in its homeostasis (Bhukhary *et al.,* 2016).

Its deficiency not only disrupts normal bone metabolism but also produces several extra-skeletal manifestations like raised incidence of cardiac diseases, impairment of psychological functions and disturbance in normal immunological development (Balion *et al.*, 2012, Szymczak and Pawliczak, 2016). During pregnancy, it is advisable to avoid vitamin D deficiency as mother has to provide an extra amount of calcium to developing fetus too. Many studies have shown several maternal and fetal complications associated with VDD in pregnancy.

India is a tropical country extending from 8.4 degree N latitude to 37.6 degree N latitude. Due to its favourable geographical location most of its areas receives adequate

sunlight throughout the year (Londhey, 2011). In countries with good sunlight availability VDD is highly unlikely but several studies have shown high prevalence of VDD in these locations (Xin *et al.*, 2017 and Aydogmus *et al.*, 2015 and Hossain *et al.*, 2011). So the aim of this review is to assess the prevalence of VDD among pregnant females in Indian population and to identify risk factors associated with it.

Physiology of vitamin D:

The two major forms of vitamin D are vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol). Vitamin D_3 is the major source of vitamin D for humans which is produced in the skin from 7-dehydro cholesterol following ultra violet light exposure while vitamin D_2 is produce by certain plants and fungi (Bruce and Carol, 2017 and Tian *et al.*, 1993). Dietary sources for vitamin D are limited which includes fatty fish, fortified dairy products, egg yolk and accounts for only 10 per cent total body vitamin D store. From the circulation, it is then carried to liver and undergoes hydroxylation to form 25 (OH) D which is the most common circulating form. Finally it is converted, again by the process of hydroxylation, to 1, 25 $(OH)_2$ D in the kidneys. It is the most biologically active form of vitamin D and is responsible for its physiological functions (Holick, 2004).

■ RESEARCH METHODS

We performed a systematic literature search of PubMed upto October 2018 for relevant articles. The terms used were "vitamin D" or "cholecalciferol" or "25-hydroxy vitamin D" in combination with "pregnancy" or "pregnant women" or "deficiency in pregnancy". Additionally, we manually search all eligible original articles, reviews and other relevant article. Studies conducted in pregnant females for vitamin D status and factors affecting its deficiency among Indian population are included in this review. The following information was extracted from each study: the first author's last name, year of publication, geographical area, sample size, diagnostic criteria for VDD, assay method to estimate level of vitamin D, the prevalence of VDD and the factors associated with it.

■ RESEARCH FINDINGS AND DISCUSSION

We found 14 studies done in different geographical areas of India for assessment of prevalence of VDD among pregnant females. There were wide variations in the methods used for the measurement of serum vitamin D level. Likewise, prevalence of VDD was also varied in different studies along with their criteria to define VDD, inadequacy or insufficiency. In this review, all these factors have been categorized and then subsequently discussed.

Vitamin D measurement method:

Radioimmunoassay (RIA) was the most common methods used in different studies to measure serum vitamin D level (Sachan *et al.*, 2005; Farrant *et al.*, 2009; Marwaha *et al.*, 2011; Goswami *et al.*, 2016 and Sharma *et al.*, 2018). Enzyme-linked immunosorbent assay (ELISA) and liquid chromatography mass spectrometry were the other two method used by some studies (Kumar *et al.*, 2015 and Sharma *et al.*, 2016).

Criteria for vitamin D deficiency and its prevalence:

With reference to the criteria and terminology used, there were quite variation in classification to define VDD, inadequacy, insufficiency or hypovitaminosis. Some studies defined hypovitaminosis as <50 nmol/l (20ng/ml) (Sachan *et al.*, 2005; Farrant *et al.*, 2009; Marwaha *et al.*, 2011 and Kumar *et al.*, 2015). Marawaha *et al.* (2011) further divided it into mild (25-50 nmol/l), moderate (12.5-25 nmol/l) and severe (<12.5 nmol/l). Whereas others had used the term VDD for the same cut off value (50 nmol/l or 20 ng/ml) (Sahu *et al.*, 2009; Dasgupta *et al.*, 2012; Singla *et al.*, 2015 and Sharma *et al.*, 2018). Level between 20-30 ng/ml was considered to be in sufficient by Sharma *et al.* (2016). In contrast to above studies, Goswami *et al.* (2016) defined VDD <12ng/ml (30 nmol/L) while Sharma *et al.* (2016) used <10 ng/ml as severe deficiency.

Due to wide variation in cut off levels, prevalence of VDD varied in different studies. When deficiency and insufficiency were combined, prevalence ranged from 56 per cent to 96 per cent. Overall, the highest prevalence was observed by Marwah *et al.* (2011) (96%) with 36 per cent having mild, 41.08 per cent having moderate and 17.7 per cent having severe VDD. Sharma *et al.* (2016) and Arora *et al.* (2018) also found high prevalence of 95.5 per cent and 93.5

Table 1: Descriptions on included studies

Author's name	Year	Place	Trimester	Sample size	Prevalence	Cut off value	Risk factors[#]
Arora, S.	2018	New Delhi	Third	200	86% deficiency 9.5% insufficiency	Not specified	Not specified
Sharma, D.	2018	Guwahati	All	250	53.6% deficiency 6.4% insufficiency	<20ng/ml deficiency 21 to 29ng/ml insufficiency	Age, BMI, sun exposure, dietary intake of calcium and vitamin D
Goswami, D.	2016	New Delhi	Second	50 singleton 50 twin	88% singleton 90% twin	<30nmol/L deficiency	Not specified
Sharma, S.	2016	New Delhi	All	418	59% insufficiency 34.44% severe deficiency	10-32ng/ml insufficiency <10ng/ml severe deficiency	Age, maternal education, husband education, socio economic status, season variation, serum calcium and phosphorus
Kumar, P.	2015	Bangaluru	Third	106	70.7% hypovitaminosis	<20ng/ml hypovitaminosis	Not specified
Singla, R.	2015	Chandigarh	Second	304	92% deficiency	<20ng/ml deficiency	Geographical area, sun exposure time, skin exposure, BMI, Socio-economic status, calcium level
Vijayendra, C.A.	2015	Hyderabad	Third	153	52.29% deficiency 35.95% insufficiency	<19ng/ml deficiency 20-29ng/ml insufficiency	Not specified
Dasgupta, A.	2012	India	first	50	42% deficiency 14% insufficiency	<20ng/ml deficiency	BMI, sun exposure, sunscreen use type of diet, dietary calcium intake, multivitamin supplementation
Sahu, M.	2009	India	Second	139	74% deficiency	<50nmol/L deficiency	Season variation, socio-economic status, education, geographical area
Farrant, H.J.	2009	Mysore	Third	559	66% hypovitaminosis 31% deficiency	<50nmol/L hypovitaminosis <28nmol/L deficiency	Age, BMI, Socio-economic status, religion calcium and vitamin D supplementation, season variation
Sachan, A.	2005	Lucknow	All	207	84.3% urban 83.6% rural deficiency	22.5ng/ml hypovitaminosis	Geographical area, religion, age, weight, dietary intake of calcium and vitamin D, sun exposure, socio-economic status

Risk factors for vitamin D level considered by authors in their study

per cent, respectively. Dasgupta *et al.* (2012) found 56 per cent of prevalence (42% deficiency and 14% insufficiency) which was lowest among the all studies. Prevalence of all the studies are summarized in Table 1. All the studies discussed in this literature were done on singleton pregnancy except the study by Goswami *et al.* (2016). They found that the prevalence of VDD was 90 per cent and 88 per cent in twins and singleton pregnancy, respectively.

Demographic, biological and life style risk factors:

Along with prevalence, most of the studies have assessed various factors associated with increased risk of VDD. None of the studies found any relation between age of the pregnant female and serum level of vitamin D. In one of the study (Singhla *et al.*, 2015) higher BMI was associated with low vitamin D level.

There is disparity of thoughts on the socio-economic status and its relation to VDD. Ferrent *et al.* (2009) found no relation while Singhla *et al.* (2015) and Sharma *et al.* (2016) identified higher and lower socio-economic status, respectively as a risk factor for VDD.

Only two studies analyzed / compared the effect of religious practices on vitamin D level (Farrant *et al.*, 2009 and Ajmani *et al.*, 2016). Burkha practice (to hide all the body with cloths except eyes) is prevalent in India among Muslim religion which prevents sun exposure. Ajmani *et al.* (2016) had reported a prevalence 76.5 per cent of VDD in Burkha clad pregnant females which was comparable to other studies involving various religious groups. Similarly there was no difference in VDD among religions reported by Farrant *et al.* (2009).

Sunlight exposure is considered to be an important factor in the synthesis of vitamin D. It is usually calculated as hours of exposure per day x per cent body surface area exposed (BSA) (Sharma *et al.*, 2018). As expected most of the studies found positive correlation between sun exposure and serum vitamin D level (Dasgupta *et al.*, 2012; Singhla *et al.*, 2015 and Sharma *et al.*, 2018). According to Dasgupta *et al.* (2012) 93 per cent of pregnant females had adequate vitamin D level if BSA was > 20% while 66 per cent females had insufficient level if BSA was < 20 per cent. Similarly Sharma *et al.* (2018) also found average BSA was 16 per cent in females with vitamin D sufficiency in compared to vitamin D insufficient females who had BSA < 8 per cent. In contrast only Sachan *et al.* (2005) reported no relation between vitamin D level and sun exposure.

Various studies have shown close association between season and serum vitamin D levels. Most of the studies found higher prevalence of VDD during winters as BSA was low due to style of clothing (Sahu *et al.*, 2009, Marwaha *et al.*, 2011, Singhla *et al.*, 2015 and Sharma *et al.*, 2016). In contrary to above studies, Farrant *et al.* (2009) found lower levels of vitamin D in summers. They assumed that during summers, because of high temperature in India, sun exposure was low but the data on sun exposure was lacking in his study.

Calcium and vitamin d supplementation is not a routine practice during antenatal care programmes in India so dietary habits should play an important role. Sachan *et al.* (2005) and Dasgupta *et al.* (2012) did not found any association with daily calcium intake and maternal serum vitamin D level. Dasgupta *et al.* (2012) also reported that non- vegetarians are less frequently associated with hypovitaminosis. In contrast, Sharma *et al.* (2018) found low intake of vitamin D and calcium was significantly associated with maternal vitamin D level. Farrant *et al.* (2009) reported a low level of vitamin D in late pregnancy even after vitamin D and calcium supplementation.

Conclusion:

This review has summarized various studies in pregnant female and concluded that even after adequate sunlight availability in India the prevalence of VDD is very high. However, cut off values and risk factors for VDD varied widely among different studies. Only few studies are available on vitamin D supplementation in pregnancy. More number of studies on vitamin D supplementation are required for better understanding of its obvious effect on prevention of VDD. Future research should focus on adequate screening for VDD, modification of risk factors and to determine how to include vitamin D supplementation during antenatal care.

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