Clinical Nutrition Experimental 28 (2019) 102–110

Contents lists available at ScienceDirect

Clinical Nutrition Experimental

journal homepage: http://www.clinicalnutritionexperimental.com

Original Article

Association of vitamin D in pregnancy and after 15 days of delivery along with neonatal

Vinit Mehrotra*, Amirita Sandhu, Ruchira Nautiyal

Himalayan Institute of Medical Sciences, Jollygrant, Doiwala, Dehradun 248140, India

ARTICLE INFO

Article history:
Received 12 June 2019
Accepted 6 October 2019
Available online 2 November 2019

Keywords:
Pregnancy
Neonatal
Delivery
Vitamin D

SUMMARY

Background &aims: India, where sunshine is abundant throughout the year, the extent of VD deficiency have been reported ranging from 50% to 86.5% for neonatal and young infants, which is still huge. The high prevalence of VD deficiency during pregnancy is increasingly recognized, especially in women, following customs like a veil. Uttarakhand located at the foothills of Himalayas is the totally socio-culturally diverse state with higher population density in the plain region like Dehradun, India.

Methods: To understand the differences in VD status we evaluated 25 (OH) D levels in three trimesters of pregnancy and at birth in neonatal serum and cord blood along with 15 days of life born within our hospital along with mother respectively.

Results: The study demonstrated a high prevalence of VD levels at the time of pregnancy. The studied reflects a deficiency of serum VD in the first trimester 18 ± 6 ng/ml, while in second and third trimester VD levels were more 38 ± 3 and 41 ± 4 ng/ml respectively as compared to first. There was a significant difference in VD status due to the presence of supplementation in both cord blood and in neonatal serum. There are many traditional factors which contributed to the observation of the high occurrence of VD deficiency in this study. Identifying VD deficiency at pregnancy time and after birth should be essential for the growth of public policy for anticipation and supplementation.

Conclusions: The study demonstrated a high prevalence of VD status with significant differences due to the existence of supplementation. There are many traditional factors which contributed to the observation of the high occurrence of VD deficiency in this study. Identifying VD deficiency at pregnancy time and after birth

* Corresponding author.
E-mail address: mehrotravinit@rediffmail.com (V. Mehrotra).

https://doi.org/10.1016/j.yclnex.2019.10.001

should be essential for the growth of public policy for anticipation and supplementation. To improve this situation, pregnant mothers should be educated about the importance of VD deficiency at and after birth for the development of risk factors.

1. Introduction

Vitamin D (VD) deficiency is a global health problem and presently 50% population is VD deficient where there is abundant sunshine throughout the year also. Recent literature and research demonstrates a soaring occurrence of VD deficiency and reported that it is not only in adult and children but also in pregnant women and their neonates [1]. Its concentration in neonates is associated with maternal VD status throughout pregnancy because the fetus is altogether dependent on the mother for VD. The active and circulating VD in the form of 25(OH)D which is stored in maternal crosses the placenta into the blood-stream of the fetus and its status at birth is highly correlated with maternal VD. An elevated predominance of VD deficiency has been reported from many global regions including northern and southern Europe, North America, the Middle East, Asia and Australasia [2,3].

The reasons for this widespread deficiency are many because (a) in metabolic and physiological processes of the human body VD is one of the essential ingredients, (b) influence the body's ability to create and absorb VD which depends on where you live, the season, how much time you spend outdoors without sunscreen, skin pigmentation, age, obesity, pollution, and having healthy intestines with optimal absorption capacity, (c) VD is consumed through fortified foods like milk, egg yolk, salmon and cod liver oil [4–6]. 75% of the Indian population consumes fortified milk or its products which are not a reliable source of VD consumption.

The lack and strategy of adequate maternal VD supplementation during pregnancy causing confusion among mothers and health care practitioners is due to different recommendations by the Health societies and Councils [7]. Literature reports that neonatal VD status is highly correlated with maternal vitamin storage and during pregnancy; women need extra amount to support her fetus, which may achieve and maintain adequate VD status as compared to other non-pregnant [8]. True vitamins are ingested, producing endogenously as produced through exogenous supplementation and these factors come in to play because it is, in fact, a misnomer which moves to other areas in the body to exert its action.

Circulating 25(OH)D is the major form of VD and is considered as the primary indicator of its status as it is essential for multiple actions in the human development and comes from skin or diet which is biologically inert and hydroxylated in the liver as 25(OH)D with a further hydroxylation in kidney as 1, 25 $(OH)_2D$ to be active.

In a country like ours, India where sunshine is abundant throughout the year, the extent of VD deficiency is still huge. The high prevalence of VD deficiency during pregnancy is increasingly recognized, especially in women, following customs like a veil. In India, studies have reported VD deficiency levels ranging from 50 to 86.5% for neonatal and young infants [9].

Uttarakhand, a state located at the foothills of a Himalayan mountain range in the northern part of India referred as God's Land is a totally socio-culturally diverse state with higher population density in a plain region like Dehradun-capital of Uttrakhand. Its extreme weather conditions had been responsible for certain negative life-style practice thus causing hypertension, diabetes, hypovitaminosis D, COPD and tuberculosis among the people. Information indicates that Socio-economic factors like unemployment, education, and poverty are common among above region that causes VD deficiency.

In order to understand the differences in VD status we evaluated 25(OH)D levels in three trimesters of pregnancy, at birth in serum & cord blood and after 15 days of life born within our hospital [Himalayan Institute of Medical Sciences, Dehradun, India] with the main objectives:

- VD status in three trimesters,
- Projected the occurrence of VD sufficiency, insufficiency and deficiency in mother and newborn at delivery,
- Neonatal levels of VD in cord blood samples and associations between VD levels at birth and after fifteen days of delivery.

To the most excellent of our knowledge, no such study among the Dehradun population is available in the literature.

2. Methods

100 healthy pregnant women and their neonates of Dehradun district receiving care at Obstetrics clinics of Himalayan Institute of Medical Sciences, Jollygrant, Dehradun were enrolled and at every trimester's blood samples and complete interview about their history and health were taken (December 2016 to February 2017). Consent in writing from each participant was obtained after explaining the nature of the project by filling a completed self-administered questionnaire included the information about VD supplements, maternal ethnicity, demography, education level, socioeconomic status, BMI, sun-light exposure related to clothing, etc and gave their approval for the analysis of cord and blood samples. Women affecting VD or calcium metabolism and twine or multiple pregnancies were excluded. The ethical clearance was obtained for the project to conduct the study. The serum samples were assayed as per period: December to February; March to May; June to August; September to November. All pregnant women were assumed to be on regular adequate supplemented VD as recommended by Gynecologists. They had received daily supplementation of 1000 mg calcium and 400 IU VD/day from 12 weeks of gestation onwards. All the neonates were born healthy from uncomplicated vaginal delivery showing no signs of distress and mothers were healthy with no chronic diseases which affect the VD status.

VD status was investigated in cord blood and serum for quantitative determination using commercially available ELISA kits by measuring the concentration of the major circulating VD metabolite 25(OH)D which reflects both dietary intake and endogenous production. The lowest sensitivity of the measurement was 0.5 ng/dl, with accuracy of 98.3% recovery and intraassay precision of CV <8% (as per CLS1 guideline EP5-A2). In the uterus, the fetus is wholly dependent on the mother with a half-life of VD approximately two months in the form of 25(OH)D which crosses the placenta into the bloodstream of the fetus [10,11].

Maternal with neonates-blood samples were drawn at the delivery time and after 15 days also. Serum was separated and kept at −20 °C for estimation. We also collected umbilical cord blood sample subsequent to postpartum from the umbilical vein after clamping. Cord blood was also collected at the time of delivery. Newborn measurements like birth weight, height, head, and neck circumference were measured at birth. Socioeconomic status was categorized according to the total score of education, occupation, and monthly per capita family income.

The establish reference values in cord blood & serum were:

Deficient: <20 ng/ml (<50 nmol/L), Insufficient: 20–30 ng/ml (50–75 nmol/L),

Sufficient/adequacy: >30 ng/ml (>75 nmol/L), Intoxication: >150 ng/ml (375 nmol/L).

3. Results

The association with demographic, socioeconomic and BMI characteristics of all the 100 Pregnant women are summarized in Table 1.

All the participants belong to Dehradun district and conceived first-time pregnancy within the age group from 25 to 30 years at Mean ± SD = 26 ± 4 years. All the neonates (63% male and 37% female)

Table 1
Association with demographic, socioeconomic and BMI characteristics of pregnant women.

Questionnaire variables	Pregnant women	
All were first time pregnant	Neonate Male (63%)	Neonate Female (37%)
Age in years	22-30 (26%)	25-30 (74%)
Residence	Rural (15%)	Urban (85%)
House hold income (Indian rupees)	2.5–5 lakhs (67%)	>5 lakhs (33%)
Education level	Graduate (72%)	Post-graduate (28%)
BMI (kg/m^2) (NV= <25.5)	20-25 (45%)	28-32 (55%)
Weight gain during pregnancy (kg)	5-10 (85%)	>10 (15%)

were healthy, born from vaginal delivery after uncomplicated pregnancies. None of them showed signs of distress at delivery and mothers were hale and hearty with any chronic diseases which influence the VD status.

Most of the subjects (54.25%) were from lower socioeconomic status. They were belonging to an urban area (85%) and 72% were graduate. The average household income in Indian rupees was approximately 5 lakhs. The participants had mean body mass index of 27 ± 4 (calculated as weight in kilograms divided by height in meters squared). Mostly all of the pregnant women gain weight (>5 kg) during the time of pregnancy.

There were total 100 neonates out of which 63% were males (boys) and rest were females (girls). The mean birth weight of neonates was 2700 ± 253 gm, the mean birth height was 43 ± 6 cm, with mean head and chest circumference 33 ± 4 cm and 29 ± 4 cm, respectively. The deliveries were assayed as into four periods: December to February; March to May; June to August; September to November.

A concentration of serum VD was observed in the first trimester as 18 ± 6 ng/ml, while in second and third trimester VD levels were more 38 ± 3 and 41 ± 4 ng/ml respectively as compared to first as shown in Table 2. With related to any season or/and month in any trimester there were no significant differences in the level of VD levels with p value more than 0.05. All the neonates were born throughout the study period December–November from vaginal delivery and were healthy.

Table 3 illustrates that VD levels in cord blood were sufficient/adequacy (mean > 30 ng/ml) while the serum neonatal at the time of delivery were insufficient (mean < 30 ng/ml). All the pregnant women had received daily supplementation of 1000 mg calcium and 400 IU VD/day from 12 weeks of gestation onwards. It was observed that the mean serum VD levels of pregnant women at the time of delivery were 40 ng/ml approximately. After 15 days of delivery the levels of VD in neonatal and their mother decreases by 15–20% and were found to be deficient/insufficient (mean > 20 ng/ml).

4. Discussion

Vitamin D deficiency has become a general community health predicament associated with many types of diseases mainly related to high risk of reduced fetal bone mineral accrual, respiratory infections and wheezing, preeclampsia, gestational diabetes and infectious disease-related in neonatal. Due to the highly significant occurrence of VD deficiency in both developed as well as in developing countries, the possible health consequences should not be underestimated as the cases of rickets is on the rise [12] and this worsens during pregnancy because of active transplacental transport of Calcium to the developing fetus [13].

To our knowledge, the present study is the first VD levels information among pregnant women and their neonates in Dehradun, Uttrakhand. Its status in the infant is closely correlated with maternal VD status during pregnancy and a high prevalence of maternal VD deficiency has been reported from many global regions including northern and southern Europe, North America, the Middle East, Asia and Australasia [14]. The study in Western populations has long-established that optimal VD supply not only influences the path of pregnancy but is also required for fetal and neonatal Calcium homeostasis, bone maturation and mineralization along with metabolic sequelae [15].

Table 2
Levels of Vitamin D at different trimesters.

	First Trimester Mean ± SD	Second Trimester Mean ± SD	Third Trimester Mean ± SD
Serum Vitamin D levels ng/ml	17.89 ± 5.9	37.89 ± 2.9	41.23 ± 3.9

In our study, the mean age of pregnant women was reported to be 26 ± 4 years and mostly was deficient of VD in expectant or first trimesters. Similar results were quoted by Rajoria and they too have found VD deficiency more in expectant females <30 years as compared to those >30 years [16].

Studies have publicized that majority of pregnant women had sub-optimal VD levels during their reproductive phase of life [17], which may be due to factors include limited sunlight exposure, reduced dietary VD and calcium intake, ethnicity, age, socio-economic status, smoking, repeated pregnancies, obesity, malabsorption syndromes, medications that increase vitamin D catabolism, and chronic liver and/or kidney disorders [18,19]. In addition, an individual's lifestyle has also been shown to influence VD status, such as the amount of exercise, reduced VD intake in the diet, biochemical indices such as triglyceride levels, factors associated with VD deficiency, and prevalence in pregnant. It was reported that plasma 25(OH)D concentrations were lower in vegetarians and vegans than in meat and fish eaters and reported that diet is an important determinant of plasma 25(OH)D [20]. Reasonably lower occurrence rates of VD deficiency during early pregnancy have also been reported from other parts of India (62%), UK (57%), Canada (39%), and Spain (18%). This high frequency worldwide of VD deficiency in pregnant women still stresses the importance of VD supplementation in early pregnancy [21].

Present study had also contributed to observe that high prevalence of VD deficiency increased due to urbanization that may be due to poor outdoor activity and greater pollution, coupled with skin pigment. There is high occurrence of VD deficiency due to lack of proper diet, poor calcium intake, community customs and remaining confined to the four walls of prehistoric housing that deprives the elderly, children and female population of the benefit of the sunshine [22].

Similar results were reported showing overall prevalence of VD deficiency in pregnant women as 84.3% and 84% in urban and rural population in northern India [23]. An extensive study of existing literature reveals widespread variation in prevalence of VD status of pregnant women, in range of environment all over the world in second trimester was 44.9% in African American and 2% in whites in USA, 50.6% in Ireland, 83.5% in turkey, 80.5% in Australia and 74.1% in India [24,25].

In our study insufficient exposure to sunlight was spectator to be a key hazard for VD deficiency and its exposure being a major cause of VD in maintaining standard 25(OH) D levels. On asking about time, 85% usually spent 15–30 min/day under sunlight with their regular cloths while only 10% spent more than 60–120 min/day as a schedule exercise. 5% were not sure about sunlight exposure. It was also observered in the present study that higher the physical activity higher the sun exposure. Two studies among pregnant women in Lucknow [24] and Mumbai [26] had found mean total body surface area % hour exposed to sun 6% and 7% h/day, respectively and reported that might be due to physiological status of study participants and urban setting in the latter studies. A study among pregnant women [27] found similar results in rural Lucknow to our finding, and it might be attributed to rural setting of both studies.

Revealing dresses and cleavage bearing cloths are frowned in customary Uttarakhand households. Pregnant women are expected to cover themselves even more and are discouraged from outdoor activity. They were not exposed to sun light due to orthodox following or conforming to the traditional or generally accepted rules or beliefs of a religion, philosophy, or practice in the family. In the present study, we found no significant association of VD between sex of the neonate, maternal age, socio-economic status, body mass index, and education level which was in line with some previous studies [28,29]. However, in Jordan, lower gestational age was found to be associated with VD deficiency in the neonate [30].

It was also observered by us that 85% had gain weight from 5 to 10 kg while 15% had gain more than 10 kg of weight at the end of pregnancy, especially between second and third trimesters. This may be due to increased intestinal calcium absorption during pregnancy which meets fetal calcium demands [31]. Cross-sectional reports have shown that in cases of severe maternal VD deficiency, serum PTH

Table 3
Levels of Vitamin D of cord blood and serum.

	Vitamin D levels (Mean) ng/ml	
	Neonate Male	Neonate Female
Cord blood	36.2	34.8
Serum neonatal at time of delivery	27.5	29.1
Serum Pregnant women at time of delivery	40.2	39.1
Serum neonatal after 15 days	17.6	19.0
Serum Pregnant women after 15 days	22.3	20.5

concentrations are increased, 1, 25(OH) 2D concentrations are decreased, and osteomalacia may occur. Observational studies and VD supplementation trials among pregnant women at high risk of VD deficiency have reported that improved neonatal handling of calcium will improve maternal VD status. Results concerning the effects of VD on maternal weight gain and fetal growth in high-risk populations are conflicting and inconclusive. There is no evidence to indicate a beneficial effect of VD intakes during pregnancy above amounts routinely required preventing VD deficiency among non-pregnant women [32].

Our study showed that in first trimesters VD levels were deficient in 89% of cases with noteworthy predictors for VD deficiency like common practices of social and cultural in Uttrakhand that stop sufficient exposure of pregnant and young women to sunshine. The major source of VD is its synthesis in dermis and epidermis, which is affected by ultraviolet B rays, including approximately 90% of the entire body need. Thus inadequate radiation or lack of UVB and in turn reduced dermal synthesis is considered as one of the main determinants of VD deficiency. All of the pregnant women were on multivitamins in between their first trimester as recommended by their consultants and were overwhelming the daily optional intake of food rich in VD as per the nutritional guidelines.

Individual's prior studies have shown that covered dress style may be an important factor affecting the prevalence of VD deficiency in pregnant women due to the religious and cultural reasons [33]. The etiology of the turn down of VD status in women is probable multifactorial, but may be due in part to increasing BMI and increased sun protection, coupled with decreased dietary intake of vitamin D, such as milk and other dairy products [34,35].

The increasing use of multivitamins and mineral dietary supplements in younger to older adults does not appear to be associated with a corresponding increase in VD concentrations [36] and clinical guidelines suggest that doses of VD more than 600 IU/day may be needed to maintain adequate plasma levels, but the appropriate standard is still debated [37]. In some randomized controlled studies, loading doses as high as 1000–4000 IU/day were needed before adequate VD plasma concentrations were measured [38].

In second trimesters VD levels were sufficient in 90% of cases because all were receiving daily supplementation of 1000 mg calcium and 400 IU VD/day along with adequate amount of sunrays and recommended intake of food for a period of more than 1–2 months as recommended by their consultant. Many women feel better during the second trimester of pregnancy as there are major changes taking place inside their bodies as their babies grow and develop. The second trimester requires essential nutrients to support that growth.

VD supplements intake was the most actionable determinant of VD status, suggesting that VD supplementation during pregnancy should receive more attention in clinical practice. Women with a diet higher in dairy, poultry and eggs had less VD deficiency in Pakistan [39] while in U.S. women with lower VD dietary intake had more deficiency [40].

In the third trimesters VD level were found to be more than second trimesters in almost (98%) all the cases perhaps owing to adequate supplementations along with daily supplementation of 1000 mg calcium and 400 IU VD/day for a period of 6–7 months. As reported through the self-administered questioner, they were taking part in daily house hold work and were more exposed to sunlight. Mostly they were taking milk and its products once in a day as suggested by their consultant. Mostly knowledge of VD was not adequate during first and second trimesters of pregnancy but our study voluntaries had briefed the VD status of the neonates' correlation with maternal VD status during

pregnancy and how fetus is totally dependent on the mother for VD. All the women became health conscious of VD deficiency and its risk factors during pregnancy.

The samples were assayed as per period: December to February; March to May; June to August; September to November and a small seasonal influence cannot be discounted. The rise in VD levels with advancing pregnancy may be a natural phenomenon similar to the rise in steroid hormones. The mean serum VD levels during the third trimester were 41 ± 3 ng/dl, which is sufficient/adequacy.

A similar finding had suggested that women receiving supplementation closer to delivery date had higher serum VD levels without a rise in fetal stores [41]. Many studies had reported that significant changes in maternal VD and calcium metabolism occur during pregnancy as to provide the calcium needed for fetal bone mineral accretion. Approximately 25–30 g of calcium are transferred to the fetal skeleton by the end of pregnancy, most of which is transferred during the last trimester [42]. The 3 possible calcium sources that may supply the mother with the necessary calcium to support fetal growth include increased intestinal absorption from the diet, increased renal conservation, and increased bone mobilization [43]. It has been estimated that the fetus accumulates up to 250 mg/d calcium during the third trimester. Data from multicentre studies specify that an overall prevalence of VD deficiency of 53% among women in the third trimester of pregnancy in Switzerland [44]. This overall prevalence is somewhat comparable with the prevalence reported in neighboring countries also, such as Germany (77%), Northern Italy (85%) or France (41%) [45,46].

Blood samples from the pregnant women and neonatal at time of pregnancy and after 15 days of delivery were collected. Umbilical cord blood samples were also collected subsequent to postpartum from the umbilical vein after clamping. It was observed that the mean serum VD levels of pregnant women at the time of delivery were 40 ng/ml approximately. Data from our study indicated that VD levels in cord blood were sufficient/adequacy (mean > 30 ng/ml) while blood sample of neonatal at the time of delivery were insufficient (mean < 30 ng/ml) because all the pregnant women had received a daily supplementation of 1000 mg calcium and 400 IU VD/day from 12 weeks of gestation onwards. All the neonates were born throughout the study period December–November from vaginal delivery after uncomplicated pregnancies and were healthy. Measurement of VD during the first and second trimester may have been beneficial because this may have allowed the commencement of supplementation earlier to enable VD levels to normalize at the time of delivery. Our results add to the evidence that cord blood VD levels strongly correlated with maternal values as reported by several studies [47,48].

We observed significantly mean serum VD levels of pregnant women at the time of delivery higher than median cord blood VD levels which differ from most of the published data [49]. A review acknowledged that the VD level in cord blood at delivery may range from 68 to 108% of maternal levels. Significantly lower median maternal VD levels compared with cord blood levels have also been reported by others; the reasons for the discrepancies are not known yet. There might be a link with the C-3 epimer concentration of the 25 (OH) D molecules that has been shown to be present especially in cord blood. This molecule involves in proliferation, differentiation, neurotrophism, neuroprotection, neurotransmission and neuroplasticity and exerts its biological function by influencing gene expression from side to side VD response elements [50,51].

Randomized clinical trials have shown that prenatal VD supplementation increases both maternal 25(OH)D and offspring birth weight [52]. It was observed from our study that after 15 days of delivery the levels of VD in neonatal and their mother decreases by 15–20% and were found to be deficient/insufficient (mean > 20 ng/ml) mostly in all cases (97%). Their may be many reasons for the same: (a) due to immense change, which includes changes in physical proportions, physiology partner support, psychiatric care and responsibility, (b) were admitted in hospital for 2–6 days or not allowed to take part in any activity of family nor allowed to come out from their rooms as a spiritual rights/ritual and not allowed to sit in sun (c) VD supplements were stopped by their gynecologists, (d) protective clothing that completely cover the body was worn by the entire sample (100%), sunscreen was used (84%) and (e) new born were only taking breast milk which contains less amount of VD.

Similar observations of VD levels had been shown in a number of longitudinal studies among breastfed infants [53,54].

5. Conclusions

The study demonstrated a high prevalence of VD status with significant differences due to the existence of supplementation. There are many traditional factors which contributed to the observation of high occurrence of VD deficiency in this study. Identifying VD deficiency at pregnancy time and after birth should be essential for the growth of public policy for anticipation and supplementation. To improve this situation, pregnant mothers should be educated about the importance of VD deficiency at and after birth for the development of risk factors.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgment

The study was funded by Uttarakhand State Council for Science and Technology, Dehradun, India by project no: UCS&T/R&D/MED-02/15-16/10937.

References

[1] Al-Daghri NM, Al-Saleh Y, Aljohani N, Sulimani R, Al-Othman AM, Alfawaz H, et al. Vitamin D status correction in Saudi Arabia: an experts' consensus under the auspices of the European society for clinical and economic aspects of osteoporosis, osteoarthritis, and musculoskeletal diseases (ESCEO). Arch Osteoporos 2017;12(1):8–15.
[2] Alladrt CL. Vitamin D in foods and as supplements. Prog Biophys Mol Biol 2018;92(1):33–8.
[3] Angurana SK. Vitamin D deficiency in children: is there a need for routine supplementation? Indian J Endocr Metab 2019; 22(5):714–5.
[4] Aparna P, Muthathal S, Nongkynrih B, Gupta SK. Vitamin D deficiency in India. J Fam Med Prim Care 2018;7(2):324–30.
[5] Arora S, Goel P, Chawla D, Huria A, Arya A. Vitamin D status in mothers and their newborns and its association with pregnancy outcomes: experience from a tertiary care center in northern India. J Obstet Gynaecol India 2018;68(5):389–93.
[6] Bowyer L, Catling-Paull C, Diamond T, Homer C, Davis G, Craig ME. Vitamin D, PTH and calcium levels in pregnant women and their neonates. Clin Endocrinol (Oxf) 2009;70(3):372–7.
[7] Ceccaldi PF, Pejoan H, Breau N, Diallo D, Ducarme G, Poujade O, et al. French prenatal Vitamin D recommended supplementation: enough or not? J Gynecol Obstet Biol Reprod 2017;46(1):35–41.
[8] Chaube D, Bhargava S. A study between relationship of vitamin d level of mother and anthropometric indices of term neonates. EJPMR 2019;6(2):622–6.
[9] Crowe FL, Steur M, Allen NE, Appleby PN, Travis RC, Key TJ. Plasma concentrations of 25-hydroxyvitamin D in meat eaters, fish eaters, vegetarians and vegans: results from the EPIC-Oxford study. Public Health Nutr 2011;14(2):340–6.
[10] Darling A, Blackbourn D, Ahmadi K, Lanham S. New, Vitamin D supplement use and associated demographic, dietary and lifestyle factors in 8024 South Asians aged 40–69 years: analysis of the UK Biobank cohort. Public Health Nutr 2018; 21(14):2678–88.
[11] Datta S, Alfaham M, Davies DP, Dunstan F, Woodhead S, Evans J, et al. Vitamin D deficiency in pregnant women from a non-European ethnic minority population: an interventional study. Br J Obstetr Gynaecol 2002;109(8):905–8.
[12] De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Sao Paulo Med J 2016;134:274–5.
[13] Divakar H, Singh R, Narayanan P, Divakar GV. Prevalence of Vitamin D deficiency and the impact of oral supplementation in an unselected pregnant Indian population. J Evid Based Med Health 2018;5(52):3589–92.
[14] Fouda MA, Turkistani IZ, Angkaya-Bagayawa FF, Krishnaswamy S, Al-Daghri N. Vitamin D deficiency in young women of childbearing age: the elephant in the room. Int J Clin Exp Med 2016;9(2):4615–9.
[15] Halicioglu O, Aksit S, Koc F, Akman SA, Yaprak I, Coker I. Vitamin D deficiency in pregnant women and their neonates in spring time in western Turkey. Paediatr Perinat Epidemiol 2012;26(1):53–60.
[16] Henderson CM, Fink SL, Bassyouni H, Argiropoulos B, Brown L, Laha TJ, et al. Vitamin D–binding protein deficiency and homozygous deletion of the GCGene. N Engl J Med 2019;380:1150–7.
[17] Hewison M, Wagner CL, Hollis BW. Vitamin D supplementation in pregnancy and lactation and infant growth. N Engl J Med 2018;379:1880–1.
[18] Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911–30.
[19] Holick MF. The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord 2017;18:153–65.
[20] Holick M, Chen T. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008;87(4): 1080S–6S.
[21] Hollis BW. Vitamin D status during pregnancy: the importance of getting it right. E Bio Med 2019;39:23–4.
[22] Hwalla N, Al-Dhaheri AS, Radwan H, Alfawaz HA, Fouda MA, Al-Daghri NM, et al. The prevalence of micronutrient deficiencies and inadequacies in the Middle East and approaches to interventions. Nutrients 2017;9(3):229–32.

[23] Jani R, Palekar S, Munipally T, Ghugre P, Udipi S. Widespread 25-hydroxyvitamin D deficiency in affluent and nonaffluent pregnant Indian women. Biomed Res Int 2014;2014:1–8.
[24] Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Ind J Med Res 2018;148:548–56.
[25] Karim SA, Nusrat U, Aziz S. Vitamin D deficiency in pregnant women and their newborns as seen at a tertiary-care center in Karachi, Pakistan. Int J Gynecol Obstet 2011;112(1):59–62.
[26] Karras S, Paschou SA, Kandaraki E, Anagnostis P, Annweiler C, Tarlatzis BC, et al. Hypovitaminosis D in pregnancy in the Mediterranean region: a systematic review. Eur J Clin Nutr 2016;70(9):979–86.
[27] Khuri-Bulos N, Lang RD, Blevins M, Kudyba K, Lawrence L, Davidson M, et al. Vitamin D deficiency among newborns in Amman, Jordan. Glob J Health Sci 2014;6(1):162–71.
[28] Kiely M, Hemmingway A, O'Callaghan KM. Vitamin D in pregnancy: current perspectives and future directions. Ther Adv Musculoskelet Dis 2017;9(6):145–54.
[29] Kochar IS, Vij V, SEthi A. Prevalence of Vitamin D deficiency in cord blood. J Clin Neonatol 2019;8:10–4.
[30] Krieger JP, Cabaset S, Canonica C, Christoffel L, Richard A, Schroder T, et al. Prevalence and determinants of vitamin D deficiency in the third trimester of pregnancy: a multicentre study in Switzerland. Br J Nutr 2018;119(3):299–309.
[31] Lind C, Chen J, Byrjalsen I. Enzyme immunoassay for measuring 25- hydroxyvitamin D3 in serum. Clin Chem 1997;43(6):943–9.
[32] McDonnell SL, Baggerly KA, Baggerly CA, Aliano JL, French CB, Baggerly LL, et al. Maternal 25(OH)D concentrations ≥40 ng/mL associated with 60% lower preterm birth risk among general obstetrical patients at an urban medical center. PLoS One 2017 Jul 24;12(7):e0180483.
[33] Mir SA, Masoodi SR, Shafi S, Hameed I, Dar MA, Bashir MI, et al. Efficacy and safety of vitamin D supplementation during pregnancy: a randomized trial of two different levels of dosing on maternal and neonatal vitamin D outcome. Indian J Endocrinol Metab 2016;20(3):337–42.
[34] Perez-Lopez FR, Pasupuleti V, Mezones-Holguin E, Benites-Zapata VA, Thota P, Deshpande A, et al. Effect of vitamin D supplementation during pregnancy on maternal and neonatal outcomes: a systematic review and meta-analysis of randomized controlled trials. Fertil Steril 2015;103(5):1278–88.
[35] Pludowski P, Holick MF, Grant WB, Konstantynowicz J, Mascarenhas MR, Haq A, et al. Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol 2018;175:125–35.
[36] Rajoria N, Gupta ML, Rajoria L, RajoriaN B. Study of association between maternal 25-hydroxyvitamin D3 level and neonatal outcome. Development 2015;6(7):8–13.
[37] Ravinder SS, Deepika C, Padmavathi R, Balakrishnan K, Vijayaraghavan J. Occurrence of vitamin D deficiency in pregnant women in South India – a preliminary study. Int J Pure Appl Biosci 2015;3:291–6.
[38] Ricca C, Aillon A, Bergandi L, Alotto D, Castagnoli C, Silvagno F. Vitamin D receptor is necessary for mitochondrial function and cell health. Int J Mol Sci 2018;19:1672–83.
[39] Roth DE, Morris SK, Zlotkin S, Gernand AD, Ahmed T, Shanta S, et al. Vitamin D supplementation in pregnancy and lactation and infant growth. N Engl J Med 2018;379:535–46.
[40] Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 2005;81(5):1060–4.
[41] Sahu M, Bhatia V, Aggarwal A, Rawat V, Saxena P, Pandey A, et al. Vitamin D deficiency in rural girls and pregnant women despite abundant sunshine in Northern India. Clin Endocrinol (Oxf) 2009;70:680–4.
[42] Saraf R, Morton SM, Camargo Jr CA, Grant CC. Global summary of maternal and newborn vitamin D status - a systematic review. Matern Child Nutr 2016;12(4):647–68.
[43] Sarma D, Saikia UK, Das DV. Fetal skeletal size and growth are relevant biometric markers in vitamin D deficient mothers: a north east India prospective cohort study. Ind J Endocrinol Metab 2018;22:212–6.
[44] Sathish P, Raveendran S, Padma R, Balakrishnan D, Muthusami M. Correlation between maternal and neonatal blood vitamin D levels and its effect on the newborn anthropometry. Int J Reprod Contracept Obstet Gynecol 2016;5:2983–8.
[45] Sharma N, Nath C, Mohammad J. Vitamin D status in pregnant women visiting a tertiary care center of North Eastern India. J Fam Med Prim Care 2019;8:356–60.
[46] Sharma S, Kumar A, Prasad S, Sharma S. Current scenario of vitamin D status during pregnancy in north Indian population. J Obstet Gynaecol India 2016;66(2):93–100.
[47] Singh RJ. C-3 epimers can account for a significant proportion of total circulating 25-hydroxyvitamin D in infants, complicating accurate measurement and interpretation of vitamin D status. J Clin Endocrinol Metab 2006;91(8):3055–61.
[48] Sotunde OF, Laliberte A, Weiler HA. Maternal risk factors and newborn infant vitamin D status: a scoping literature review. Nutr Res 2019;63:1–20.
[49] Velusamy P, Devarajulu K. Prevalence of vitamin D deficiency in exclusively breast fed infants. Int J Contemp Pediatr 2019;6(2):299–301.
[50] Wagner CL, McNeil R, Hamilton SA, Winkler J, Rodriguez Cook C, Warner G, et al. A randomized trial of vitamin D supplementation in 2 community health center networks in South Carolina. Am J Obstet Gynecol 2013;208(2):e1–13.
[51] Thiele DK, Ralph J, El-Masri M, Anderson CM. Vitamin D3 supplementation during pregnancy and lactation improves vitamin D status of the mother-infant dyad. J Obstet Gynecol Neonatal Nurs 2017;46(1):135–47.
[52] Whiting SJ, Calvo MS. Vitamin D fortification and supplementation policies to correct vitamin D insufficiency globally. In: Feldman D, Pike WS, Bouillon R, Giovannucci E, Goltzman D, Hewison M, editors. Vitamin D, Volume 2: health, disease and therapeutics. 4th ed. London: Academic Press; 2018. p. 91–108.
[53] Wise SA, Phinney KW, Tai SS, Camara JE, Myers GL, Durazo-Arvizu R, et al. Baseline assessment of 25-hydroxyvitamin D assay performance: a vitamin D standardization program (VDSP) interlaboratory comparison study. J AOAC Int 2017;100(5):1244–52.
[54] Shen Y, Pu Liuyue, Si Shuting, Xin X, Mo M, Shao B, et al. Vitamin D nutrient status during pregnancy and its influencing factors. Clin Nutr 2019. https://doi.org/10.1016/j.clnu.2019.06.002. Available online 8 June 2019.